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RHEUMATOID ARTHRITIS

The Importance of a Comprehensive Approach in Treatment

Chairman's Address

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The cause of rheumatoid arthritis remains unknown. Although many theories have been proposed, no one of them has been generally accepted. To date, there is no method of treatment for rheumatoid arthritis which can be considered "specific"—a term which implies rapid and complete reversal of subjective and objective manifestations of the disease, whether localized to the skeletal system or other parts of the body. Until this long-awaited discovery is at hand, the treatment of rheumatoid arthritis is necessarily confined to those measures believed to be beneficial but not necessarily of proved value. It is the purpose of this report to review briefly the nature of the disease, to outline the minimal requirements for the assessment of newer methods of treatment and to stress the importance of a comprehensive approach in the treatment of patients with this disease.

NATURE OF THE DISEASE

Rheumatoid arthritis presents a variety of clinical forms and pursues no single pattern of development. It must be regarded as a distinct disease entity that can readily be recognized. Space does not permit more than a listing of the outstanding features that distinguish rheumatoid arthritis from other forms of joint disease. It is essential to realize that one is dealing with a generalized disease with well marked constitutional manifestations that are not merely secondary to the articular lesions. Female subjects are more commonly affected than male, except in cases in which the spine is involved. The onset is not limited to any age group and may occur from infancy to senility. The constitutional symptoms often precede the appearance of objective joint signs, and it is thus possible to surmise the diagnosis in what may be termed a prodromal stage. Precipitating factors, such as physical or emotional strain, infection and accidental or operative trauma, often appear to play a role both in the initiation of the prodromal symptoms and in the production of articular manifestations of the disease. The type of onset ranges from the insidious to the explosive, with endless variations between. In many patients the initial complaints are fatigue, exhaustion, lassitude, loss of weight and symptoms referable to the nervous system and the vasomotor apparatus. In cases of severe disease these symptoms may be profound. Both large and small joints are affected, at first perhaps in a migratory fashion but later with unrelenting persistence. Examination of the joints reveals no early observations that are specifically different from those of other forms of arthritis. The signs of inflammation, usually mild and often accompanied with effusion, almost always precede the development of limitation of motion and deformity. More important is the symmetric polyarticular distribution of the arthritis, although involvement of one or a few joints is not uncommon in the early stages. Muscular weakness and atrophy are prominent, and inflammation of muscles and extra-articular fibrous tissue is almost invariably present. Subcutaneous nodules form a characteristic part of the clinical picture in about 20 per cent of the cases. Involvement of other organs of the body is evidenced in certain cases by cold, clammy hands and feet, atrophy and pigmentation of the skin, lymphadenopathy and splenomegaly, pericarditis and pleuritis and ocular changes including iritis, uveitis, scleritis and scleromalacia perforans. The course of the disease is all too often one of steady or intermittent progression, although complete or nearly complete remissions are not unusual at first, and certain patients recover without significant residual disability.

The laboratory studies, although not of diagnostic help, may aid in the determination of the severity of the disease. The sedimentation rate of the red cells and the Schilling or filament-nonfilament count are useful in following the course of the disease, but only occasionally in differential diagnosis. In approximately 50 per cent of the cases, the serum of patients with rheumatoid arthritis agglutinates strains of hemolytic streptococci of Lancefield group A in a characteristic manner. In such cases, a positive reaction to a test is of value in distinguishing rheumatoid arthritis from other forms of arthritis in which agglutinations are encountered only rarely. Unfortunately, the reaction to the test is rarely positive in patients having the disease less than one year. The antistreptolysin and antifibrolysin titers in rheumatoid-arthritis serums are not characteristic, whereas rheumatic fever serums usually show elevated values. Biopsy of subcutaneous nodules is frequently of aid in differentiating the former disease from the latter. Examination of synovial fluid is helpful in ruling out traumatic arthritis, degenerative joint disease and the specific infectious arthritides. Hypochromic anemia is also observed in cases of severe disease. The white blood cell count varies considerably. In most cases, it is within normal limits or only slightly elevated. In the acute and active stages, counts of 12,000 to 20,000, occasionally higher,

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may be observed, whereas in cases of long-standing chronic disease definite leukopenia may develop. Roentgenograms in joint disease must always be interpreted in the light of the duration, severity and articular distribution. With the aid of such facts, accurate roentgenologic diagnosis of rheumatoid arthritis is usually possible. The characteristic features include soft tissue swelling, effusion, systemic decalcification of bones, loss of bony substance in "punched-out" areas, narrowing or even obliteration of the joint space, marginal erosion and, finally, subluxation and gross bony destruction. No single feature mentioned constitutes a diagnostic criterion, and it has been truly said that the picture differs from that of specific infectious arthritis largely in speed of progression.

Postmortem examinations confirm the systemic nature of rheumatoid arthritis, inflammatory lesions being demonstrable in the skin, subcutaneous tissue, muscles, peripheral nerves, eyes and serous membranes, as well as the articular tissues. Such widespread involvement of nonarticular systems serves to stress the importance of a comprehensive approach in the treatment of patients with this disease.

ASSESSMENT OF NEWER METHODS OF TREATMENT

Patients with chronic diseases of unknown cause are frequently subjected to various therapeutic procedures that are of questionable merit and are usually based on conjecture. Such supposedly curative and ameliorative measures are regularly administered to patients with chronic rheumatoid arthritis, often at considerable expense, not infrequently with resulting complications, occasionally even death, and generally without material benefit to the patient. This state of affairs is due in part to the fact that patients with chronic diseases often demand treatment. They are ever hopeful that each new form of treatment prescribed will be as specifically curative as the advertisements claim. There are, however, other causes for the continued prescribing of many useless antirheumatic remedies. The premature publication of poorly controlled studies acclaiming great therapeutic benefits and voluminous medical advertising constantly confront the busy practitioner of medicine. He has neither the time nor the facilities to investigate adequately the claims made. Except for the reports of the Council on Pharmacy and Chemistry of the American Medical Association, its "Queries and Minor Notes" columns and the all too infrequent publications concerning the repudiation of previously published premature claims, the busy physician has no way to determine the respective merits of these therapeutic procedures.

In a chronic disease of unknown cause, such as rheumatoid arthritis, characterized by unpredictable spontaneous remissions and exacerbations, it is extremely difficult to evaluate the results of treatment with any degree of certainty unless the studies are rigidly controlled. Because of the decided variations in the course of the disease from case to case, each patient must be made to serve as his own control. If studies pertaining to the evaluation of therapeutic procedures are not conducted in this manner, one is likely to conclude that the improvement observed is the result of treatment, whereas it may actually represent the natural variation in the course of the disease. Such a controlled study can be made only by choosing patients whose clinical course and variations in sedimentation rate have been known for months or years prior to the institution of a new form of treatment. An adequate follow-up period is most essential, so that one can decide as to the permanency of any improvement noted during the period of treatment. In addition to these precautions, it is extremely important that the patient be kept on the same basic regimen before, during and after the administration of the treatment being evaluated. Every available means should be employed in evaluating clinical improvement. One should record separately the subjective, objective and laboratory evidence of improvement, the final results being based on all three. In addition, one must judge the total severity of the disease. This is done by taking into consideration the degree of constitutional symptoms and signs, the speed of progression of the disease, the amount of disability, the extent of the involvement and the activity of the process. This method of recording enables one to establish more accurately what, if any, psychic effect must be taken into account in the final summation. In all fairness to the type of treatment being studied, only patients whose disease state is active and still reversible should be selected. That the activity of the disease process is reversible is shown both by spontaneous remissions and by those encountered in pregnancy and intercurrent jaundice. One must also realize that in the early and atypical cases there are more likely to be remissions than in the more typical cases which have been more or less stationary for a long time. If the administration of a given form of treatment should result regularly in improvement in this latter group, one might have reason to suspect that one is dealing with a specific form of treatment.

The early enthusiasm for each procedure is sooner or later dampened by the publication of critical well controlled studies, of the type outlined, with essentially negative results.[1] The exception is gold therapy, introduced nearly twenty years ago, although its acclaimed specificity has occasionally been challenged in recent years. Studying the efficacy of gold therapy in the manner described reveals that it cannot be regarded as a specific and constantly effective treatment for rheumatoid arthritis.[2] It is more difficult to state whether gold is of some benefit to the patient with rheumatoid arthritis and whether its use is therefore justified in a patient failing to respond to conservative measures. Two control studies apparently demonstrate an additive therapeutic effect on the part of gold during relatively brief periods of observation.[3] Otherwise, the results obtained with gold may be approximated with those in patients given general conservative treatment. A careful follow-up study of patients improving during gold therapy reveals a high percentage of relapses, so that the net gain is slight. There is even an indication that the natural fluctuant course of the disease is largely responsible for the results reported in such cases. The burden of proof is still on the proponents of gold therapy to demonstrate by adequately controlled studies with a follow-up of three to five years that a significant effect is exerted on the course of rheumatoid arthritis by the administration of gold salts.

Gold therapy, like certain other antirheumatic drugs, is not without danger. The toxic manifestations are

1. Abrams, N. R., and Bauer, W.: Treatment of Rheumatoid Arthritis with Large Doses of Vitamin D: Critical Evaluation, J. A. M. A. **111**: 1632-1639 (Oct. 29) 1938. Freyberg, R. H.; Block, W. D., and Promer, M. S.: Study of Sulfur Metabolism and Effect of Sulfur Administration in Chronic Arthritis, J. Clin. Investigation **19**: 423-435, 1940. Sidel, N., and Abrams, N. J.: Treatment of Chronic Arthritis: Results of Vaccine Therapy with Saline Injections Used as Controls, J. A. M. A. **114**: 1740-1742 (May 4) 1940.

2. Short, C. L.; Beckman, W. W., and Bauer, W.: Gold Therapy in Rheumatoid Arthritis, New England J. Med. **235**: 362-368, 1946.

3. Fraser, T. N.: Gold Treatment in Rheumatoid Arthritis, Ann. Rheumat. Dis. **4**: 71-75, 1945. Sashin, E.; Stanbuch, J., and Kling, D. H.: Gold Therapy in Rheumatoid Arthritis, J. Bone & Joint Surg. **21**: 723-734, 1939.

unpredictable, unpreventable and, at times, irremediable. If the specificity of gold were established, this risk would be justifiable in a disease that bears the implications of lasting invalidism. With the case as yet unproved for its place as a palliative or adjuvant remedy in rheumatoid arthritis, the hazard of this form of treatment should furnish the decisive argument against its general use.

Dependence on any one therapeutic agent in the treatment of rheumatoid arthritis, unless it has a degree of specificity comparable to that of the sulfonamide drugs and penicillin in lobar pneumonia, deprives the patient of the benefit of constitutional treatment, physical therapy, orthopedic measures and other indicated therapeutic procedures.

IMPORTANCE OF A COMPREHENSIVE APPROACH

It is obviously impossible to select a true control series of untreated patients with rheumatoid arthritis. Nearly every patient with the disease in a recognizable form has received some form of treatment whether advised by his physician or someone else. Therefore, the advocates of a conservative therapeutic regimen, consisting largely of bed rest, psychotherapy, adequate analgesia, exercises to improve or maintain muscle and joint function, application of heat to actively involved joints, proper support for joints to allow reduction of muscle spasm and pain, the prevention and correction of deformities and an adequate diet, with supplementary vitamins when indicated and iron and transfusions when necessary,[4] cannot prove that it alters the natural course of rheumatoid arthritis. Two hundred and fifty unselected patients with the disease who received this type of treatment were observed for an average period of ten years.[5] Of this series, 23, or 9.2 per cent, were reported as five-year "cures" ("remissions" or "arrests")—a slightly higher figure than the 6.3 per cent recently reported for 142 patients given gold therapy.[6]

The systemic nature of the disease indicates that measures to increase the patient's resistance and place him in the best general health, in addition to proper handling of the inflamed articulations to promote healing and to preserve function, are in order. This is no easy task. It requires a full appreciation of the nature of the disease, the personality of the person afflicted and the importance of detailed management, as well as an abundance of patience, equanimity, ingenuity and resourcefulness on the part of the physician. Failure to approach the problem in this manner is frequently the cause of considerable frustration on the part of the physician treating patients with rheumatoid arthritis. If this reaction is not recognized, it may unconsciously impel the physician to resort to an endless number of therapeutic agents until such time as the patient wanders off to another physician, the use of patent remedies or quacks. Resort to methods of doubtful value may at times be necessary to hold the patient to the pursuit of a few simple measures of proved worth. In such instances, the physician should admit compromise with his intellectual honesty and admit that by doing so, he hopes to tide the patient over a discouraging period when the disease seems to be at a standstill or progressing in spite of all efforts. The possibility of a remission when things look darkest should never be lost sight of. The startling freedom from symptoms gained from intercurrent hepatic jaundice or pregnancy points out that the process is not irreversible and that the long-awaited specific method of treatment may yet come to light.

Once the diagnosis has been made, the patient should know what is ahead of him and should be informed that there is no easy and rapid road toward arrest of the disease. He should also be made acquainted with the natural course of rheumatoid arthritis, so that he will not relax his precautions as a result of a remission or become overly depressed from an exacerbation.

The proper treatment of rheumatoid arthritis necessitates consideration of the patient as a human being. Attention must be given, not only to the many psychogenic factors that played a role in the precipitation and the progression of the arthritis, but also the various problems produced by the disease. There must be a realization that whatever emotional instability previously existed is increased by the illness. The effect of the financial load caused by the sickness and of the disruption of activity and of plans must be handled. At all times an attempt must be made to understand what the patient thinks about the disease, to be aware of and lessen his fear of it and to increase his insight into the effect of psychogenic factors on the course of the disease.

CONCLUSION

The treatment of patients with rheumatoid arthritis requires an understanding of the systemic nature of the disease, its many clinical manifestations, its varied clinical course and the persons afflicted. Until the advent of a specific therapeutic agent, treatment of this disease necessitates a comprehensive approach of the type briefly described.

4. Short, C. L., and Bauer, W.: The Treatment of Rheumatoid Arthritis, New England J. Med. 227: 442-450, 1942.
5. Short, C. L., and Bauer, W.: The Course of Rheumatoid Arthritis in Patients Receiving Simple Medical and Orthopedic Measures, New England J. Med. 238: 142-148, 1948.
6. Ragan, C., and Tyson, T. L.: Chrysotherapy in Rheumatoid Arthritis: Three-Year Study of One Hundred and Forty-Two Cases, Am. J. Med. 1: 252-256, 1946.

RENAL PTOSIS AND ITS TREATMENT

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A listless meeting of urologists can be suddenly animated by the simple word "nephropexy." This usually will bring forth varying shades of opinion, many of which are extreme. The proponents of the operation will cite figures to show that the percentage of patients cured by this operation is as high as, or indeed higher than, that following most surgical procedures. In their opinion, the poor results from nephropexy result from improper selection of patients or poor surgical technic. The opponents of the operation are equally convinced that nephropexy results in only a small percentage of cures and that the failures are an inherent property of an ill conceived operation.

The urologic literature contains numerous reports which are enthusiastic about the brilliant results achieved by nephropexy. It will suffice to refer to but two of these reports. Mathé,[1] employing a technic for nephropexy which he devised in 139 cases, was able to cure or relieve 98.7 per cent of the patients. Postoperative pyelographic studies carried out in 71 cases revealed successful fixation of the kidney in 100 per

Read before the meeting of the Hollywood Academy of Medicine, Los Angeles, Nov. 13, 1947.
From the Section on Urology, Mayo Clinic (Drs. Braasch and Greene), and the Mayo Foundation (Dr. Goyanna, Fellow in Urology).

1. Mathé, C. P.: The Present-Day Status of Nephropexy and End Results in Three Hundred and Eighty-Four Operative Cases, Urol. & Cutan. Rev. 41: 772-779 (Nov.) 1937.

cent. Woodruff and Scherer[2] employed a radically different technic for nephropexy in a group of 59 patients and were able to cure or relieve 98.3 per cent. Furthermore, postoperative urographic studies of 48 of the patients disclosed successful fixation of the kidney in 100 per cent of the cases. Other authors have reported equally good results using different surgical technics, usually their own. It is, therefore, obvious that a number of patients are reported as cured or relieved by nephropexy performed with radically different technics. However, for some reason, few papers have been published that report doubtful results from the surgical treatment of nephroptosis. On inquiry many urologists, as well as general surgeons, employing similar surgical technics, admit that they seldom advise nephropexy because the postoperative results in their cases often are unsatisfactory. Since the surgical technic is not a fundamental factor, it is evident that the proper selection of the patient is the most important factor in the treatment of the condition.

What is the proper method of selecting patients for nephropexy? This seems to be difficult to define, and little help is obtained from the literature. This statement was made by one advocate of nephropexy: "Nephropexy is indicated when pain, gastrointestinal symptoms or nervous symptoms are due to ptosis." This is vague and of little help when one is confronted with the individual patient. It may be extremely difficult to determine whether the patient's symptoms are the result of the renal ptosis or simply coincidental. It would seem, therefore, that a clinical review of a series of patients who had nephroptosis, with an attempt to correlate the objective findings and subjective symptoms, should aid in the proper selection of patients for nephropexy. With this objective in mind, we present the following study of cases of renal ptosis encountered at the Mayo Clinic and cite our experience with nephropexy. Although our experience with renal ptosis is large, our experience with nephropexy performed at the clinic is small.

Material for this report comprises 230 cases in which a diagnosis of renal ptosis had been made at the clinic with the aid of excretory or retrograde urography. In most instances ptosis was demonstrated by making the excretory urogram with the patient in the upright position. Only cases of simple ptosis or ptosis complicated by minor degrees of pyelectasis, without other evidence of obstruction at the ureteropelvic juncture, were included in this study.

CLINICAL CONSIDERATIONS

Renal ptosis is not an abnormal condition and does not cause symptoms per se. It is only when complications develop that symptoms may arise.

On reviewing our series of cases of nephroptosis we found that the diagnosis was made most frequently in women in the third to the fifth decade. The majority of these women were thin or decidedly underweight. Many of them complained of symptoms which were so variable that they could not be relied on as accurate indications of a renal lesion. These symptoms included a dragging sensation in the abdomen, nervousness, backache, nausea, vomiting and other complaints suggestive of an irritable colon. The type and localization of pain often were ill defined, so that it was difficult or impossible to decide whether the pain could be attributed to renal ptosis. The symptom given most attention was definite intermittent pain referred to the renal region, with anterior and downward radiation, brought on by unusual exercise or hard work and relieved by lying down. A comparatively few patients complained of severe pain which could be regarded as typical of renal colic. Approximately 20 per cent of the patients complained of urinary symptoms such as frequency, dysuria and nocturia, which on cystoscopy were found to be of local origin, since renal infection was present in but few. Approximately a third of the patients had no symptoms which were related in any way to the kidneys. Many of these patients had discovered or had been told that they had an abdominal mass, but otherwise they were asymptomatic. In other instances an abdominal mass was discovered at the time of our physical examination and subsequent urologic investigation identified it as a manifestation of renal ptosis.

In view of the ill defined symptoms in most of these cases, we concluded that further objective evidence of renal pathologic change secondary to nephroptosis was essential before surgical treatment could be considered. For this purpose we found that the urographic examination offered many data which were of clinical interest and diagnostic value.

The Degree of Renal Ptosis.—It is often regarded that the degree of renal ptosis may be a factor in causing symptoms or evidence of renal obstruction.

TABLE 1.—*Grade of Nephroptosis in 230 Cases*

Side Involved	Nephroptosis, Grade				Total
	1	2	3	4	
Right	30	57	62	5	154
Left	5	0	0	0	5
Bilateral	6	28	30	7	71
Total	41	85	92	12	230

For purposes of clarity, we have divided renal ptosis into four grades, based on the degree of descent of the kidney. The normal position of the renal pelves is generally considered to be opposite the first or second lumbar vertebra, with the right kidney slightly lower than the left. We have arbitrarily classified as renal ptosis, grade 1, those cases in which the renal pelvis is situated opposite the third lumbar vertebra. In grade 2 ptosis the pelvis is opposite the fourth lumbar vertebra, whereas in grade 3 ptosis the pelvis is opposite the fifth lumbar vertebra; cases in which the renal pelvis is situated below the fifth lumbar vertebra are designated as ptosis, grade 4.

In more than three fourths of the cases in our series ptosis was graded 2 or 3 (table 1). Ptosis involving the right kidney alone was most common and was present in two thirds of the cases. In the remaining third the condition was nearly always bilateral. Ptosis limited to the left kidney was uncommon.

We next sought to determine whether a relationship existed between the degree of renal ptosis and the presence of pyelectasis. In would be conceivable that the further the kidney descends from its normal position, the more interference with normal drainage there would be, resulting in pyelectasis and delayed emptying time. Actually, however, this assumption was shown to be wrong. The incidence of pyelectasis and delayed emptying time was approximately equal in the first three grades of ptosis and less frequent in grade 4, in which ptosis was most marked (table 2).

We then sought to determine whether a relationship existed between the degree of ptosis and the patient's

2. Woodruff, S. R., and Scherer, R. G.: Renal Ptosis, J. Urol. 35: 125-134 (Feb.) 1936.

symptoms (table 3). It was found that the patient complained of symptoms which might be attributed to the kidney with equal frequency, irrespective of the grade of ptosis. We also found that all grades of ptosis could be present and the patient could still remain asymptomatic. From these data it is evident that the degree of ptosis is of little or no clinical importance. In other words, the fact that the kidney is below the crest of the ilium or is freely movable in the abdomen offers no evidence as to the advisability of nephropexy.

Urography.—Urography is of vital importance in the clinical examination of nephroptosis. It will determine the degree of ptosis and malrotation, the presence of pyelocaliectasis with evidence of urinary retention, and the comparative renal function. These data may be acquired in three ways; namely, by means of the excretory urogram, the retrograde urogram and the delayed urogram. The urogram is of particular importance in visualizing a minor degree of pyelocaliectasis which has been regarded as more or less typical of renal ptosis. The descriptive term "flabby pelvis" has been applied to it. The dilatation may be predominant in the calyces, although usually the pelvis is also involved. Although borderline pyelectasis may be visualized only in the retrograde pyelogram, this may be reversed and the excretory urogram may bring out details of deformity better than are brought out by the retrograde urogram. Sometimes pyelectasis can be seen best in a urogram made in the erect position. It may be visualized more accurately in a late delayed urogram than in the simple urogram.

TABLE 2.—*Relationship Between Grade of Nephroptosis and Incidence of Pyelectasis or Delay in Emptying Time*

Grade	Total Cases	Pyelectasis or Delay in Emptying Time	
		Cases	Per Cent
1	41	11	27
2	85	23	27
3	92	28	30
4	12	1	8

What is the explanation of this borderline pyelocaliectasis, this "flabby pelvis"? Pyelectasis may be the result of either dynamic or adynamic factors. In other words, it may be caused by actual obstruction or by physiologic impediment to excretion.

One of the following factors may be present: (1) obstruction at or near the ureteropelvic juncture, intermittent and of moderate degree; (2) adynamic or atonic dilatation resulting from a previous renal infection; (3) imbalance of the renal innervation, with consequent atony.

That pyelectasis, in many of these cases, is not caused by actual obstruction may be shown by (1) the absence of retained fluid in the renal pelvis, as ascertained through ureteral catheterization; (2) the absence of retained medium shown in the ten minute delayed film, and (3) surgical exploration.

In many cases of renal ptosis the borderline pyelectasis may not be apparent on surgical exploration and no cause for obstruction of the pelvis may be found. In contrast, when actual obstruction at or near the ureteropelvic juncture is present, the pyelectasis is quite evident on exploration and the retained urine usually drains readily when the cause of the obstruction is removed.

Chronic renal infection without actual ureteral obstruction may cause a moderate degree of pyeloureterectasis. As the result of infection the submucosal tissues of the renal pelvis and ureter often become abnormal, with resulting atrophy. Since in most cases of renal ptosis no renal infection is present, it would seem that adynamic pyelectasis may be ascribed in most cases to an atony of the renal pelvis caused by disturbed renal innervation. As a result, inadequate renal drainage and possible retention of urine follow. This condition is found so frequently in association with nephroptosis that some evidence of retention other than urographic deformity is desirable. This evidence was furnished, in our series of cases, by the delayed urogram, which offers an important means of determining retention of urine in the renal pelvis.

Delayed urograms are made by retrograde injection of contrast medium into the renal pelvis. The catheter is then withdrawn and roentgenograms are made at ten minute intervals. If the opaque medium persists in the renal pelvis fifteen minutes or more after withdrawal of the catheter, the delayed emptying time would indicate inadequate renal drainage. The delayed urogram is of particular value in the presence of the borderline pyelectasis frequently observed in renal ptosis. Unfortunately, however, the method does not differentiate between dynamic and adynamic pyelectasis.

Since adynamic retention may be present without causing pain or any other symptoms, delayed renal drainage does not prove that this is the cause of the patient's complaints. However, unless the existence of stasis can be visualized in nephroptosis, surgical intervention usually is not indicated. Theoretically, therefore, if the shadow of the opaque medium remains in the delayed urograms in which there is evidence of the so-called borderline or flabby pelvis of nephroptosis, nephropexy would be indicated provided the symptoms and other clinical factors warrant.

SURGICAL TREATMENT

Nephropexy was performed at the Mayo Clinic on 21 patients with primary nephroptosis during the decade from 1935 through 1944. During this period more than 1,000,000 patients were examined at the clinic and more than 400,000 underwent operation. Nephropexy was employed only when the patient's symptoms and evidence of impaired renal drainage apparently were caused by renal ptosis. In most of the patients borderline pyelectasis or delayed renal drainage was demonstrated.

TABLE 3.—*Relationship Between Grade of Nephroptosis and the Presence or Absence of Symptoms Referable to the Kidney*

Grade	Total Cases	Unclassified	Asymptomatic		Symptomatic	
			Cases	Percentage	Cases	Percentage
1	41	2	9	22	30	73
2	85	3	23	27	59	69
3	92	2	34	37	56	61
4	12	0	3	25	9	75

A variety of technics was employed in performing nephropexy. In most instances, the renal capsule was reflected from the kidney and sutured to the erector spinæ or lumbar muscles. In other instances, the capsule was employed as a sling. In a few cases, sutures were placed between the intact capsule and the fascia of the lumbar muscles. The suture material employed was either chromic surgical gut or ribbon gut. In 6

instances, denervation of the renal pedicle was performed simultaneously with nephropexy. The value of this procedure could not be determined, but since 3 of the patients in whom denervation was performed failed to get any relief of symptoms and since our experience with this operation in other types of cases has not been particularly reassuring, it would seem questionable whether it could be as important as some surgeons seem to think.

Nephropexy was performed in numerous other instances, either secondary to, or in conjunction with, other surgical procedures about the kidney. These cases were not included in the report, inasmuch as more than one surgical procedure was carried out and the value of nephropexy alone could not be determined. Nephropexy was performed more or less as a routine procedure after plastic repair for obstruction at or near the ureteropelvic juncture. It also was performed in many instances secondary to pelviolithotomy, to division of obstructing anomalous renal vessels or tissue bands and to renal malposition. These cases are not included in this report, although it cannot be denied that in some cases nephroptosis may have been an etiologic factor.

Results of Nephropexy.—Of the 21 patients who underwent nephropexy, 11 experienced more or less subjective relief from their symptoms; 10 patients were not subjectively benefited by the operation. Of the 11 patients with favorable results, only 3 had complete and permanent relief. In the other 8 cases the original pain was largely relieved, but other symptoms continued. A correlation could not be found between the degree of ptosis and the subjective results of nephropexy. It was noted that the incidence of pyelectasis or delay in emptying time was somewhat greater in the group of patients who received good subjective results.

It is difficult to explain the difference between our postoperative results—more than 50 per cent failure—and those achieved by urologists previously cited. It certainly was not due to failure of surgical technic, since the preoperative degree of ptosis was found to exist in only 1 of our patients examined after operation. It is possible that some of the uniformly good results claimed by some urologists were based on postoperative improvement reported within a few months after nephropexy. Several of our patients who reported no relief said they were much improved during a period of six months to a year after operation, but later symptoms similar to the previous ones returned. In 2 of our unimproved patients subsequent extrarenal complications developed to explain their pain. In 1 of these 2 patients acute disease of the gallbladder developed a year later, and cholecystectomy relieved the patient of her former symptoms. At the time of her clinical examination at the clinic the cholecystogram revealed no abnormality. The other of the 2 patients died a year later, and autopsy revealed a diffuse carcinoma involving the head of the pancreas, the liver and the gallbladder. These lesions were missed completely in spite of a careful clinical examination. Another patient without relief after nephropexy underwent nephrectomy elsewhere about two years later. Subsequently she reported that she had the same symptoms as before. It is evident that her symptoms, which we thought were typical of renal origin, had nothing to do with the kidney.

It is possible that we are somewhat pessimistic as to the results from nephropexy because of the many patients observed at the clinic who had had this operation performed elsewhere. Most of these patients came with symptoms similar to those that existed prior to operation, in spite of the fact that the kidney was successfully anchored. Many of these patients had experienced temporary relief of symptoms after nephropexy, and then either the former symptoms returned or other complaints developed. To complicate the situation, in several patients who had been subjected to nephropexy elsewhere with relief of so-called renal symptoms, our urographic studies showed that the kidney which had been operated on had fallen to its preoperative low position. In another patient a right nephropexy had been performed elsewhere with relief of symptoms, but pyelograms and delayed urograms showed evidence of retention in both renal pelves. From this it was evident that atonic renal retention could be present without actual obstruction and without causing any symptoms. It is not unusual for patients who have been subjected to nephropexy to say that their symptoms have switched to the other kidney, in spite of the fact that the other kidney may be normal in position and function.

Many patients said that they had undergone elsewhere several operations prior to nephropexy, without relief of symptoms. Certainly one should hesitate before advising nephropexy on a patient who has already had cholecystectomy, appendectomy and possibly hysterectomy.

It is surprising how many patients with renal ptosis were benefited by means of palliative and corrective measures. Although renal pads, corsets or other types of abdominal support may not keep the kidney in place, yet many of these patients stated that such support gave them much relief. The relief can be explained either on psychologic grounds, on the basis of counterirritation or on the grounds that lumbosacral pain often is helped by some form of back support. Other measures, such as increased and nourishing diet, reduction in work and periods of rest and recreation, were of definite help in some cases, particularly if a gain in weight was effected. Psychosomatic treatment has benefited many and, if skillfully employed, may be the key to recovery. Many patients were included in this list who were in the menopause and who stated that their improvement became permanent after this period had been passed.

According to these observations, it would be no exaggeration to say that the problem of nephroptosis is not a simple one. It is evident that any one who advises nephropexy without careful and thorough consideration of all the factors involved and without giving the patient the benefit of other methods of treatment is doing that patient an injustice. The number of patients with nephroptosis who present clinical data which clearly indicate nephropexy is exceedingly small. These data should include not only intermittent pain with definite renal radiation, but also urographic evidence of borderline pyelectasis and delayed renal drainage. Even with this careful selection, no assurance of permanent relief of symptoms after nephropexy can be made. The fact that a few carefully selected patients have been benefited may justify the operation in occasional cases.

SUMMARY AND CONCLUSIONS

Nephroptosis occurs most frequently in thin, underweight women and most commonly affects the right kidney. Nephroptosis is not necessarily an abnormal condition, since it is present in a large number of cases, causing no symptoms or evidence of renal pathology.

The subjective symptoms accompanying renal ptosis are so variable and ill defined that they offer an uncertain guide in determining whether renal ptosis is an

etiologic factor. No correlation could be found between the varying grades of ptosis and the symptoms which might possibly be related to the kidney. Borderline pyelectasis, the so-called flabby pelvis, is often observed to be associated with renal ptosis.

Delayed renal drainage may be demonstrated in many cases by the delayed urogram. No correlation could be found in our series of patients between the varying degrees of ptosis and the presence or absence of pyelectasis or delay in emptying time.

Most patients with nephroptosis will be benefited by nonoperative measures.

Even in cases in which the symptoms point directly toward a renal origin, urographic data, such as evidence of a borderline pyelectasis or delayed drainage, should be required before nephropexy is considered.

Although evidence of delayed renal drainage, such as borderline pyelectasis and retained medium as observed in the delayed urogram, does not necessarily indicate obstruction, yet nephropexy is advisable only when such evidence is present, combined with symptoms of definite renal origin.

The fact that the symptoms were relieved in less than 50 per cent of our patients subjected to nephropexy after careful selection would, in itself, make one hesitate before advising this operation. A conservative attitude is substantiated by the fact that many patients observed at the clinic had previously undergone nephropexy elsewhere without relief of symptoms.

SURGICAL AND ROENTGENOLOGIC ASPECTS OF DUODENAL DIVERTICULA

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Much has been written concerning the frequency of occurrence of duodenal diverticula.[1] Too little stress, however, has been placed on the fact that in certain cases these diverticula cause symptoms which may be cured by surgical intervention. We agree that the majority of these lesions are innocuous and asymptomatic, but, on the other hand, we concur with Alesen [2] that symptoms do occur with sufficient frequency to cause the clinician and surgeon to keep this entity in mind.

We report 3 cases in which symptoms were eliminated by resection of the diverticula. One of the cases was of unusual interest, because the diverticulum contained an active ulcer in its base and because it occurred in the third portion of the duodenum. No such case to our knowledge has been reported. Most duodenal diverticula are situated adjacent to the ducts of Wirsung or Santorini, in the second portion of the duodenum.

ROENTGENOLOGIC ASPECTS

The manifestations of a diverticulum of the duodenum are essentially the same as those of a diverticulum occurring elsewhere in the alimentary tract.[3] The main characteristics are those of an outpouching, usually from the mesial wall of the second portion of the duodenum, connecting to the small intestine by means of a stalk. A single sac is usually present, but multiple outpouchings may occur.[4] The diverticulum varies in size from several millimeters to 7 or 8 cm. As a general rule it is easily movable under the palpating finger, as observed during fluoroscopy. Studies of stasis, at twenty-four hours and forty-eight hours, often show a retention of the barium sulfate in the diverticulum.

In the roentgenologic differential diagnosis one must consider:

1. *Pseudo or Prestenotic Diverticulum.*—This deformity occurs with an ulcer of the first portion of the duodenum. The ulcer commonly has its origin in the duodenal bulb, and one can usually identify a niche or a crater.

2. *Localized Distention of the Second and Third Portions of the Duodenum.*—Such distention may be produced by a tight superior mesenteric vessel, which may present a picture suggesting true sacculation. Similar dilatation may occur at the point of trifurcation of the gastric omental sac, where it forms the hepaticoduodenal ligament, the duodenocolic ligament and the hepaticoduodenocolic ligament. In both these conditions a stalk is not present. The enlargement is continuous with the long axis of the bowel. Furthermore, these dilatations can be readily recognized when the patient is examined both in the prone and the supine position. When the patient lies on his back, the distention of the duodenum becomes pronounced; when he assumes the prone position, the distention will be lessened or disappear entirely.

3. *Malignant Condition.*—Occasionally an annular carcinoma must be differentiated. In carcinomatous lesions there is distortion and discontinuity of the small bowel mucosa, whereas in a diverticulum the mucosa is continuous and undisturbed. The rarity of a malignant condition of the duodenum has been reported elsewhere.[5]

4. *Benign Tumors.*—A benign tumor is usually not confused with a diverticulum. As a rule it casts a negative shadow in contrast to the usual homogeneous dense shadow, produced by a diverticulum filled with barium sulfate.

In our experience, diverticulum of the duodenum occurred in 1.5 per cent of all patients examined.

CLINICAL ASPECTS

It is characteristic that patients exhibiting symptoms all have one symptom in common; i. e., distress during or after eating. Nearly all have been previously treated for ulcer or have submitted to surgical treatment for supposed disease of the gallbladder or appendix. Some have definitely been labeled as psychoneurotic in spite of a long history of dyspepsia and positive roentgeno-

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logic evidence of duodenal diverticula. It is our belief that patients who present a history of dyspepsia, characterized by pain and fulness after meals, and in whom diverticula can be demonstrated radiologically, should be entitled to surgical extirpation of the lesion, if other causes have been eliminated. We feel that these patients should not be operated on until the history, physical

Fig. 1 (case 1).—*A*, preoperative roentgenogram. This shows a typical large diverticulum projecting from the mesial wall of the ascending limb of the duodenum (third part), demonstrating both the pouch and the stalk. On fluoroscopy, the diverticulum filled readily. Despite deep digital palpation, it could not be emptied. The diverticulum measured 3 cm. by 3.2 cm. The stalk measured 0.6 cm in diameter. *B*, roentgenogram taken twenty-four hours preoperatively. The stomach has completely emptied. Only fragments of the mediums are seen in the upper part of the small intestine. However, there was almost complete retention of the meal in the diverticulum. The stalk was again demonstrated, but its communication with the third portion of the duodenum was not seen on this hourly examination, thus indicating that the pouch did not affect the transit of the meal through the duodenal loop.

examination and roentgenologic and laboratory studies have eliminated other factors that could produce these symptoms, and, certainly, no patient should be operated on solely because of roentgenologic evidence of the diverticulum. In the following case reports, it will be noted that these criteria have been adhered to.

REPORT OF CASES

Case 1.—A 48 year old business executive, who complained of dyspepsia and epigastric pain intermittently for fifteen years prior to examination, had been told previously that he had a duodenal ulcer. At various times he had been treated with alkalies, antispasmodics and ulcer diets. On occasion, he had been relieved by this treatment, but the symptoms always recurred with the slightest deviation from this routine. For the past year, in spite of rather rigorous conservative management, the patient had persistent pain and stated that he constantly suffered from indigestion. Roentgenographic examination (Conti) revealed a large diverticulum of the third portion of the duodenum (fig. 1).

At operation the diverticulum was resected (Stevens and Foltz) without opening of the duodenum. The pathologic report revealed acute and chronic diverticulitis with ulceration of the base.

Postoperative convalescence was uneventful. The patient at the time of writing had remained asymptomatic for approximately one year. Roentgenograms showed a normal duodenal pattern (fig. 2).

Case 2.—A 33 year old fireman was admitted to the hospital on May 25, 1945, for medical observation. His chief complaint was that of epigastric pain following eating, which had persisted for some months despite medical treatment. Roentgenograms showed a small diverticulum of the duodenum. Because it is the general belief that a diverticulum of this size rarely produces symptoms, medical treatment was instituted, and the patient was kept under close observation. However, the symptoms persisted. At the patient's request, surgical exploration was done (Stevens and Foltz) on July 11. The diverticulum was not evident; therefore the duodenum was opened longitudinally, and a diverticulum about 2 cm. deep was seen adjacent to the accessory pancreatic duct. The diverticulum was inverted and excised. The incision in the duodenum was closed transversely. Pathologic examination revealed ulceration of the base of the diverticulum, with polymorphonuclear and round cell infiltration. Convalescence was uneventful. The patient was completely asymptomatic following the operation and had remained so for the six months that follow-up was possible.

Case 3.—A pharmacist's mate second class was admitted to the hospital on Oct. 23, 1945, with the chief complaint of epigastric pain following meals, which had persisted for four years prior to examination. In addition, nausea was present with the onset of the pain and, on many occasions, vomiting occurred shortly after the onset. There was a complaint of a tight full feeling in the upper part of the abdomen for about twelve hours following one of these typical attacks. In September, roentgenologic studies had revealed a duodenal diverticulum, when the patient was admitted to the hospital for operation. The patient's past history revealed that in January 1944 a cholecystectomy had been performed, with no relief of symptoms. Results of the physical examination were essentially negative throughout, except for some slight tenderness in the upper right quadrant of the abdomen. At operation (Stevens) the diverticulum was not seen until the duodenum was opened. A diverticulum adjacent to the duct of Wirsung was then seen, extending 1 inch (about 2.5 cm.) into the pancreas. The operative procedure was similar to that in case 2, opening the duodenum longitudinally, inverting the diverticulum and excising. The duodenum was closed transversely. Exploration had been done elsewhere, because of a roentgenologic diagnosis of duodenal diverticulum, and the diverticulum had not been observed. The pathologic report revealed a diverticulum lined by glandular mucosa, having a well marked muscularis mucosa and mucous glands under the muscularis mucosa resembling Brunner's glands, with chronic inflammatory exudate between the glands. The postoperative convalescence was uneventful, and the patient had remained free of symptoms for the three months during which follow-up was possible.

Fig. 2 (case 1).—Postoperative roentgenograms. It is apparent that there was no residual deformity of the duodenum and that the diverticulum was completely resected.

SUMMARY

Three cases of duodenal diverticula are reported. All 3 patients presented symptoms of dyspepsia, pain during or after eating and positive roentgenographic evidence of duodenal diverticula. Surgical extirpation of the diverticula afforded complete relief in all 3 cases, all other measures having failed. In 1 of these cases an ulcer was present in the base of the diverticulum. This diverticulum was located in the third portion of the

duodenum. In 2 cases the diverticulum could not be located until the duodenum was opened, because the diverticulum was a hidden projection into the pancreas.

CONCLUSIONS

1. The majority of duodenal diverticula do not produce symptoms and require no treatment.
2. Some diverticula of the duodenum produce symptoms which may be cured by surgical treatment.
3. It is sometimes necessary to open the duodenum to locate a diverticulum at operation.

EXCESSIVE HYPOPROTHROMBINEMIA DUE TO "DICUMAROL"

Its Treatment with Lyophilized Plasma

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Twenty to 25 per cent of persons who receive "dicumarol" in the treatment of thromboembolic disease are hyperreactors to the drug, in that the conventional dosage produces an excessive elevation of the prothrombin time to levels at which hemorrhage may occur.[1] Bleeding takes place in approximately 6 per cent and is of major importance in 1 to 2 per cent, with occasional fatalities being reported.

Two therapeutic measures have been used in the management of dangerously elevated prothrombin times. First, large parenteral doses of synthetic vitamin K in the form of menadione sodium bisulfite [2] or vitamin K_1 oxide [3] have been shown to reduce an excessive elevation of prothrombin time to safe range within twelve to forty-eight hours in approximately 85 per cent of persons. It thus appears that the results of this form of therapy are apparent only after a significant interval and may not occur at all in certain patients. Second, transfusions of whole fresh blood or fresh plasma have been employed when actual bleeding is taking place because of the delay and occasional failure to respond to the massive dosage of vitamin K. Some investigators [4] have stated that no beneficial effect in reducing the prothrombin time or the degree of bleeding results from transfusion. Others [5] report favorable results of transfusion both in lowering the prothrombin time and in decreasing the hemorrhagic tendency, with the recommendation that repeated transfusion may be necessary due to the transitory effect.

It was believed that the use of lyophilized plasma warranted a clinical trial in cases of hemorrhage associated with excessive hypoprothrombinemia due to "dicumarol" because lyophilized plasma, reconstituted with 0.1 per cent citric acid and distilled water, has been shown by Strumia [6] to possess a normal prothrombin content comparable with that of fresh whole blood. In addition, 500 cc. of plasma would have the equivalent effect of 1,000 cc. of whole blood in reducing the prothrombin time, inasmuch as the effective factors in combating the hypoprothrombinemia are considered to be situated in the plasma.

Although current sources of pooled lyophilized plasma introduce the potential risk of homologous serum hepatitis, this form of therapy has certain advantages that warrant consideration. In the first place, the general availability of this material where blood banks are not at hand justify its employment. Furthermore, problems of grouping do not arise in patients in whom sudden hemorrhage demands immediate control.

It is the purpose of this report to record observations on the efficacy of lyophilized plasma in reducing the excessive hypoprothrombinemia occurring in the course of "dicumarol" anticoagulant therapy.

MATERIALS AND METHODS

Determinations of prothrombin time were performed on whole plasma, according to a modification [7] of Quick's technic,[8] with commercially supplied rabbit lung as the source of thromboplastin, 0.1 molar sodium oxalate as the anticoagulant and 0.025 molar calcium chloride. Normal prothrombin time in this laboratory with the technic employed was found to be 14 (± 2) seconds. The percentage of normal prothrombin activity was determined from a logarithmitic prothrombin activity curve constructed according to Quick.

"Dicumarol" was administered in accepted dosage of 300 mg. on the first day, 200 mg. on the second day and subsequent daily dosage depending on the results of the prothrombin time of that day. It was attempted to prolong the prothrombin time to an optimal reading of 27 seconds, which is 20 per cent of normal activity. The effective therapeutic range was

TABLE 1.—*Prothrombin Time and Activity of Random Samples of Reconstituted Lyophilized Plasma* *

Specimen	Whole Plasma Prothrombin Time (Seconds)	Percentage of Normal Prothrombin Activity
1	13.5	100
2	15.1	75
3	14.9	80
4	12.7	100+
5	15.1	75
6	14.0	100+
7	14.1	100
8	14.2	97
9	15.1	75
10	15.0	78
11	14.9	80
12	14.7	87
13	15.1	75
14	14.4	90
15	15.0	78
16	14.5	90

* Red Cross.

From the Departments of Medicine and Surgery, Columbia University College of Physicians and Surgeons, and The Presbyterian Hospital.

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considered to be between 22 and 44 seconds, which is respectively 30 per cent and 10 per cent of normal activity. In this series of patients with thromboembolism who were treated with anticoagulants, hemorrhage has rarely occurred below 44 seconds, 10 per cent of normal activity.

RESULTS

The previous observations [8] on the prothrombin content of lyophilized plasma were confirmed. It was noted that the prothrombin activity of these random samples averaged between 75 per cent and 100 per cent of normal (table 1).

On the basis of this finding, lyophilized plasma in doses of 500 cc. was administered to patients in whom an excessive hypoprothrombinemia had occurred during "dicumarol" therapy. The results in 13 patients are presented in table 2. In this group hemorrhage of significant severity was not taking place at the time of transfusion, so that observations as to the effect of the plasma on actual bleeding were not possible. The lyophilized plasma was effective in producing an immediate reduction of prothrombin time to safe range. It was apparent that an upswing toward the pretreatment level occurred as soon as six hours in some

TABLE 2.—*Changes in Prothrombin Time (Seconds) Following of Lyophilized Plasma in Patients with Hypoprothrombinemia Due to "Dicumarol"*

Patient	Before Plasma	After Plasma: Immediate	3 Hours	6 Hours	9 Hours	15 Hours	20 Hours
1	58.0	27.8	31.8	....	....	47.5	....
2	43.0	26.5	....	....	....	36.0	....
3	43.0	29.8	27.0	27.6	....	....	33.5
4	54.2	27.6	34.9	38.7	....	58.5	....
5	92.0	35.6	39.4	49.0	67.0	....	....
6	67.0	28.6	....	30.9	....	33.7	....
7	76.1	32.5	37.5	47.0	....	....	....
8	90.0	....	35.0	45.0	....	....	60.0
9	67.5	27.4	....	....	....	37.4	....
10	78.0	31.4	27.3	32.1	....	....	....
11	50.5	29.5	36.5	38.2	....	....	....
12	69.0	38.0	37.5	42.0	....	....	....
13	85.0	30.0	34.5	....	....	38.5	....

patients, similar to the transient effects following whole blood transfusion as previously reported.[9] It is thus evident that, pending the more permanent but delayed effects of vitamin K, repeated plasma infusions may be essential to maintain a prothrombin time in the safe range.

SUMMARY

It has been confirmed that lyophilized plasma, reconstituted with 0.1 per cent citric acid solution, contains normal prothrombin activity. This plasma is effective in producing an immediate reduction of prothrombin time to safe range in persons with excessively elevated levels due to administration of "dicumarol." Effective reduction in prothrombin time may be maintained for as little as six hours, thus necessitating multiple transfusions in certain instances. Pooled lyophilized plasma should be employed only when grouped fresh blood is not available owing to the added risk of transmission of homologous serum hepatitis.

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EFFECT OF UREA ON BACTERICIDAL ACTION OF SULFONAMIDE DRUGS

Report of Five Cases of Bacterial Meningitis

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In 1942 Tsuchiya [1] and his co-workers reported in vitro experiments with urea and the sulfonamide compounds which indicated that the inhibitory effect of sulfadiazine on the growth of Escherichia coli is significantly increased by the presence of urea, even when methionine, a sulfonamide inhibitor, is present.

They extended their observations to other sulfonamide compounds, using para-aminobenzoic acid as the sulfonamide inhibitor, and also showed that three strains of sulfathiazole-resistant staphylococci in a synthetic medium were susceptible to urea-sodium sulfathiazole combinations. They attributed this beneficial effect of urea to its inhibition of the sulfonamide inhibitors and to an enhancement of the bacteriostatic action of the sulfonamide compounds.

The development of sulfonamide resistance by bacteria has become significant, and any agent which may overcome this resistance may play an increasingly important role. McLeod [2] showed that the development of sulfapyridine fastness in a strain of Pneumococcus type I is accompanied by a greatly increased production of sulfonamide inhibitor. Schmidt [3] and his co-workers have shown that strains of Pneumococcus type I and type III can be made resistant to sulfapyridine in vitro and in vivo in mice. Vivino and Spink [4] reported 2 cases of staphylococcic bacteremia, both strains becoming markedly sulfonamide resistant, one after only eight days of therapy.

The mechanism of bacterial inhibition by the sulfonamide compounds may be due to a depression of the enzyme reaction in the bacterial cell. Green [5] has produced bacterial extracts containing a proliferation factor which powerfully stimulates the reproductive rate of many bacteria, and it is believed that this proliferation factor stimulates the same enzyme reaction in the bacterial cell which sulfonamide compounds inhibit. The sensitivity to sulfanilamide of any bacterial strain may be conditioned by the rate at which the autolysing organism liberates this "P" factor. The effect of urea on this factor is unknown. It is known that urea renders sulfonamide compounds more soluble and that it also has a solvent action on pus, debris and necrotic tissue which act as sulfonamide inhibitors.[6] Urea has the additional advantages of being relatively nontoxic.

Mr. Alfred Reich cooperated in the bacteriologic studies.
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mildly bacteriostatic, diuretic, simple to administer and inexpensive.[7]

Clinical reports appeared which tend to confirm the laboratory experiments. Schnitker and Lenhoff[8] employed urea and sulfadiazine or sulfathiazole in the treatment of 40 patients with sulfonamide-resistant gonorrhea, among whom 52.5 per cent cures were reported. However, they administered only 30 Gm. of urea orally daily, which by present standards is a minute dose.

In 1945 Ecker[9] reported his experiences with the use of urea and the sulfonamide compounds in the successful treatment of a case of meningitis due to Esch. coli which failed to respond to penicillin and sulfadiazine.

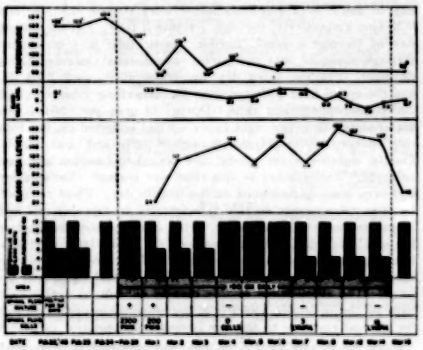
In 1946, Vesell, Gross and Sussman[10] reported the use of urea and sodium sulfadiazine intravenously in the successful treatment of a case of subacute bacterial endocarditis which had failed to respond to sulfadiazine alone. They stressed the importance of increased solubility of sulfadiazine in the urine with reduction of sulfadiazine crystalluria when urea is given with massive doses of sodium sulfadiazine.

REPORTS OF CASES

CASE 1.—A man, aged 43, contracted meningitis due to Alcaligenes faecalis after the breaking down of his operative wound following removal of a large sacral meningocele. For three months after operation large doses of sulfadiazine orally and penicillin intramuscularly and intrathecally were given in an attempt to prevent localized meningitis at the operative site from spreading. However, on Dec. 26, 1945, A. faecalis was grown from spinal fluid. Despite the continued use of sulfonamide compounds and penicillin intramuscularly and intrathecally, spinal fluid cultures remained positive and the patient's condition grew steadily worse. Streptomycin was then tried by intrathecal injection; although this drug temporarily sterilized the spinal fluid it had to be discontinued because of excruciating leg pain when injected into the lumbar subarachnoid space, and head pain when injected into the cisterna magna. By Feb. 28, 1946, the patient was in extremis. Up to this time he had received a total of 39,256,000 units of penicillin intramuscularly and 12,546,000 units intrathecally, 347.5 Gm. of sulfadiazine orally and intravenously, and 200,000 units of streptomycin intrathecally.[11] He was then started on urea, 30 Gm. orally every four hours, and penicillin was continued as before, 30,000 units intramuscularly every three hours. Sulfadiazine, which had been discontinued four days previously, was again started, 2 Gm. every four hours.

Temperature returned to normal in twenty-four hours and culture of spinal fluid was sterile four days after starting urea. Cell count in the spinal fluid dropped from 2,300 polymorphonuclear cells to zero in that time. Spinal fluid on two subsequent examinations was sterile; one specimen contained 3 lymphocytes and one 15 lymphocytes. The patient became alert and after fifteen days of this therapy was discharged (the chart). The patient returned to his job one month later and has remained well. Blood urea during urea therapy ranged from 24 mg. per hundred cubic centimeters to a maximum of 180.[12] The only symptoms attributed to the elevated blood urea were somnolence and loss of appetite. Blood sulfadiazine level ranged from 4.1 mg. per hundred cubic centimeters to 16.5 before urea was given and a maximum of 13.5 after it was started. The response in this case was dramatic and undoubtedly due to the combined use of urea and sulfadiazine.

CASE 2.—A man, aged 53, contracted meningitis due to Klebsiella pneumoniae after removal of an acoustic neurinoma on Sept. 12, 1946. Because the mastoid process was entered during the operation he was given a prophylactic course of penicillin, 30,000 units intramuscularly at three hour intervals for six days. Because of continued fever a second course of penicillin was started on the fifteenth postoperative day. On the eighteenth postoperative day, spinal puncture disclosed viscid, brown, turbid fluid which on culture grew K. pneumoniae. Accurate cell count could not be made. He was started on sulfadiazine, 1 Gm. every four hours. On the twentieth postoperative day penicillin was discontinued and 30 Gm. doses of urea every four hours were started with sulfadiazine dosage continued as before.[13] Six days after starting this therapy spinal fluid culture was still positive, but on the ninth day it was sterile, temperature reached normal and therapy was stopped. He was discharged four days later. He returned to his job and was in good health when seen six months after discharge. The recovery in this case was unequivocally due to the combination of urea and sulfadiazine, as the patient received no other therapy during the period of response.



The chart shows the effect of introducing urea into the therapy of case 1. Similar records were kept for the other cases.

CASE 3.—A man, aged 31, on July 16, 1946, sustained a compound, comminuted skull fracture in the right parietal region extending into the right petrous bone, with resulting cerebrospinal fluid rhinorrhea and otorrhea, and Bell's palsy on the right side. His scalp wound was sutured. Sulfadiazine in doses of 1 Gm. orally every four hours and penicillin 30,000 units intramuscularly every three hours were started as a prophylactic measure. On the seventh day the otorrhea ceased, and the scalp wound was found to be infected. Lumbar puncture on the eighth day revealed a pressure of 290 mm. water, and the fluid contained 1,600 polymorphonuclear cells with Esch. coli on culture. A secondary debridement of the scalp was performed and urea was started in doses of 30 Gm. orally every four hours in addition to the sulfadiazine which the patient was already receiving. Penicillin was discontinued, a total of 2,160,000 units having been given. Fifty thousand units of streptomycin was injected intrathecally at twelve hour intervals on the first four days of urea therapy. These injections always caused severe leg pain and were discontinued. On the third day of urea therapy spinal fluid culture was

7. Weinstein, L., and McDonald, A.: Effect of Urea, Urethane and Other Carbamates on Bacterial Growth, Science **101**: 44-45 (Jan. 12) 1945. Neter, E. R., and Clark, P.: Combined Antimicrobial Activity of Urea and Sulfathiazole in Urine, J. Urol. **51**: 101-109 (Jan.) 1944.

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9. Ecker, A. D.: Urea and Sulfonamide Treatment of Bact. Coli Meningitis, Lancet **1**: 176-177 (Feb. 10) 1945.

10. Vesell, H.; Gross, I. H., and Sussman, R. M.: Urea as an Adjunct to Sulfonamide Therapy: Report of Its Successful Use in Case of Subacute Bacterial Endocarditis, J. Lab. & Clin. Med. **31**: 444-452 (April) 1946.

11. This patient had several generalized convulsions twelve days after the intrathecal injection of streptomycin and while receiving penicillin intrathecally. He has had petit mal attacks since his discharge until recently.

12. On one occasion simultaneous samples of blood and spinal fluid revealed blood urea of 111 mg. per hundred cubic centimeters and spinal fluid urea of 193 mg. per hundred cubic centimeters.

13. The bitter taste of urea was masked somewhat by giving it in cold fruit juice.

still positive, but it was sterile on the fifth day and on three subsequent examinations. Sulfadiazine and urea were discontinued after fifteen days of therapy and the patient was discharged. In this case the patient contracted meningitis due to Esch. coli while on penicillin and sulfadiazine. Spinal fluid cultures remained positive during the administration of streptomycin and subsequently became sterile while the patient was receiving urea and sulfadiazine.

Case 4.—A boy aged 6 months contracted an infection of the respiratory tract on March 17, 1947. On March 18, his temperature was 105 F. and he began vomiting. On March 22 he had a generalized convulsion. He was hospitalized and a diagnosis of pneumococcic meningitis was made. He was given 2 Gm. of sulfadiazine daily, and 20,000 units of penicillin intramuscularly every three hours and 25,000 units intrathecally daily. There was gradual improvement, and the spinal fluid cell count dropped from 25,000 to 10. He was discharged on April 12.

On April 24 symptoms of meningitis recurred. He was transferred to Cleveland Clinic on April 28. His temperature was 104 F., the anterior fontanel was bulging, there was spasticity of the extremities, and moderate opisthotonus. Ventricular fluid on this date contained 500 polymorphonuclear cells and 102 mg. protein and grew Staphylococcus albus. On the day of entry, urea and sulfadiazine were started, 0.5 Gm. and 0.25 Gm. respectively, through a stomach tube. On the second day of therapy a small, flexible, plastic tube was introduced through a needle into the lumbar spinal canal for continuous drainage. On the third day the temperature was 102.4 F., and the spinal fluid collected from the indwelling tube contained 300 polymorphonuclear cells. Dosage of urea and sulfadiazine was reduced to every eight hours. Fluid collected on the fifth day contained 150 polymorphonuclear cells and was sterile. On the eighth day the plastic tube ceased to function and was removed. Temperature at this time was normal. Sulfadiazine and urea were discontinued on the twelfth day. Fluid removed by cisternal puncture on the sixteenth day contained 1 cell and 33 mg. protein, and was sterile. The patient was discharged on the eighteenth day and was last seen six weeks later. At this time he was found to have some neurologic sequellae of the infection but the anterior fontanel was soft and there was no fever. The significance of this case is difficult to evaluate in view of the debatable identity of the responsible organism, but the clinical response to therapy is unquestionable.

Case 5.—A girl aged 5 months was admitted to Cleveland Clinic on May 20, 1947, for treatment of congenital communicating hydrocephalus. In preparation for operation, continuous spinal drainage was instituted by means of a small, flexible, plastic tube introduced through a needle into the lumbar spinal canal on the third hospital day. A benzalkonium chloride dressing over the tube became contaminated with feces, and on the eleventh day temperature rose to 104.5 F. The anterior fontanel was tense. Fifteen thousand units of penicillin intramuscularly every three hours was started. Temperature remained elevated and on the thirteenth day the tube in the spinal canal was removed, as it had ceased to drain. Ventricular fluid contained 58 polymorphonuclear cells but was sterile. Penicillin was discontinued on the fifteenth day because of failure to control the fever. On the sixteenth day ventricular fluid contained no cells but grew Esch. coli on culture. On the twenty-second day ventricular fluid again grew Esch. coli, and sulfadiazine and urea, 0.2 Gm. and 0.5 Gm. respectively, were administered every three hours through a stomach tube. On the twenty-fourth day ventricular fluid was still positive for Esch. coli and contained 51 polymorphonuclear cells. Temperature became normal on the twenty-sixth hospital day, although the fluid culture remained positive until the thirtieth day. An operation for hydrocephalus was carried out on the thirty-fifth day. Urea and sulfadiazine were discontinued two days later when the temperature became normal. The patient was discharged on the ninth postoperative day with no evidence of infection. The response to the therapy in this case was unequivocal.

SUMMARY

We have successfully treated with urea and sulfadiazine a case of meningitis due to Alcaligenes faecalis which did not respond to penicillin and sulfadiazine, and in which streptomycin was not tolerated; a case of meningitis due to Klebsiella pneumoniae, which developed while the patient was receiving prophylactic doses of penicillin; 2 cases of meningitis due to Escherichia coli as well as a case of meningitis probably due to Staphylococcus albus. Since this form of therapy is simple, safe and effective it should be tried in sulfonamide-resistant infections before resorting to streptomycin.

A case of tuberculous meningitis and 1 case of meningitis due to Torula failed to respond to urea and sulfadiazine.

AUREOMYCIN: A NEW ANTIBIOTIC WITH VIRUCIDAL PROPERTIES

I. A Preliminary Report on Successful Treatment in Twenty-Five Cases of Lymphogranuloma Venereum

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As a result of a comprehensive screening program at the Lederle Laboratories Division, American Cyanamid Company, a substance has been obtained from a Streptomyces which gave promise of possessing unusual antibiotic properties. The antibiotic has been named aureomycin, and a statement regarding its specific properties and chemical purification will be published elsewhere.[1] Of special interest to us was the striking spectrum of activity exhibited by this antibiotic against many rickettsiae and certain viruses.[2] In particular, it was noted that aureomycin was highly effective in the treatment of mice infected intracerebrally with the virus of lymphogranuloma venereum.

In view of the information made available to us concerning the unusual therapeutic range of aureomycin, it seemed desirable to use this antibiotic in human beings suffering from lymphogranuloma venereum. An added incentive to the study was the realization that effective treatment has not been available for this disease. Although claims have been made for the efficacy of numerous compounds,[3] including various sulfonamide drugs, antimony potassium tartrate, penicillin and stibophen ("fuadin"), it is generally agreed that only secondary infections are affected by the compounds in question, whereas the basic disease process due to the viral agent remains untouched.

Since a large percentage of the patients acutely afflicted with this virus disease become chronic sufferers of a progressive, fibrotic and destructive process, the need to provide specific therapy is apparent. Twenty-five cases of lymphogranuloma venereum were selected for this study and were divided into three groups: (1) buboes, (2) lymphogranulomatous proctitis, with or without ulceration, and (3) benign cicatricial rectal strictures.

Dr. V. Subbarow gave us suggestions throughout the course of this study and supplied the aureomycin that was used.

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1. Duggar, B. M., and Hesseltine, C. W.: Personal communication to the authors.
2. Wong, S. C., and Cox, H.: Personal communication to the authors.
3. Wright, L. T.; Freeman, W. A., and Bolden, J. V.: Lymphogranulomatous Strictures of Rectum, Arch. Surg. 53: 499-544 (Nov.) 1946.

METHOD OF STUDY

Manner in Which the Cases Were Followed.—1. History: A detailed history was taken, with special emphasis on the initial appearance and progress of the local lesion.

2. Physical Examination: A complete physical examination was made which embraced (*a*) examination of local lesion by observation, palpation and mensuration, (*b*) proctoscopic examination in rectal cases wherever possible, (*c*) biopsies in all cases where possible and (*d*) aspiration of buboes with touch preparations, smears and cultures.

3. Laboratory Studies: The laboratory studies carried out were: (*a*) urinalyses, (*b*) hematologic studies—red blood cell count, white blood cell count, hemoglobin estimation and hematocrit determinations, (*c*) Kahn tests of the blood, (*d*) chemical studies of the blood—determinations of urea nitrogen, creatinine, glucose plasma proteins, albumin-globulin ratio, alkaline and acid phosphatase, (*e*) Frei tests, (*f*) complement fixation tests for lymphogranuloma venereum, (*g*) tests of hepatic function—icteric index, Van den Bergh, thymol turbidity and cephalin flocculation tests, (*h*) bone marrow smears, (*i*) serum levels of aureomycin before and after treatment, (*j*) bacteriologic cultures, (*k*) smears for inclusion bodies, (*l*) histologic examination of biopsy material and (*m*) barium enemas in cases of rectal stricture. For every patient a detailed history was taken and complete physical examinations were made. Examination of urine, red and white blood cell counts, hemoglobin estimation, Kahn test, Frei test and urea nitrogen, creatinine and glucose determinations were made in all cases. The other tests were done in a sufficient number of cases to give us adequate information as to possible harmful effects that the drug might have.

4. Drug Administration: Aureomycin, as furnished by the Lederle Laboratories, is a yellowish crystalline substance in sterile sealed vials containing 20 mg. A special diluent furnished with the drug was used in our early cases. In our later cases, the drug was dissolved in 2 cc. of isotonic sodium chloride solution. The intramuscular route of injection was used. Daily dosage in some cases was 10 mg., in some cases 20 mg. and in 1 case 40 mg.

CASES STUDIED

Buboes Due to Lymphogranuloma Venereum.—There were 8 patients in this group with buboes due to lymphogranuloma venereum, all of whom were Negro men. Their ages varied from 22 to 31 years. The specific lesions had been present in 7 cases two weeks to two months and in 1 case for two years. In 7 patients the bubo was the only pathologic observation, while 1 patient had associated proctitis with rectal bleeding. The nodes varied in size from that of a large pea to that of an egg and were unilateral in all instances. The nodes were removed in 5 cases, and the histologic observations were compatible with lymphogranuloma venereum. Aspiration biopsy for smears and cultures were bacteriologically sterile. Smears for inclusion bodies were made in all cases.

Reactions to Frei tests were positive in all patients with buboes. The reaction to the complement fixation test for lymphogranuloma venereum was 4 plus in a 1:40 dilution in 2 cases. (A butchers' strike at this time made it impossible to obtain sheep cells for the other cases.) The Kahn reaction was 2 plus in one instance and 4 plus in another. Six reactions to Kahn tests were negative. The results of urinalyses were normal throughout the study. Urea nitrogen, creatinine, sugar and plasma protein determinations remained within normal limits throughout the period of the study. Albumin-globulin ratios remained unchanged. In 5 of these cases, after treatment, the following tests of hepatic function were carried out: icteric index, Van den Bergh, thymol turbidity and cephaline flocculation tests. All observations were normal. The treatment for 7 of the patients in this group consisted of a single daily intramuscular injection of 20 mg. of aureomycin. In 2 of the cases the patients were given one injection of 20 mg. of aureomycin into the bubo along with the regular treatment.

RESULTS

All patients showed a reduction in the size of the gland after four days of treatment with aureomycin, an event which in our experience over twenty-four years with several hundred cases of early lymphogranuloma venereum has never occurred spontaneously within so short a time. The patient that had rectal bleeding in addition to the bubo reported no further rectal bleeding after three days of treatment with aureomycin (table 1).

Effect of Aureomycin on Cellular Inclusions.—When properly coordinated with clinical and laboratory observations, the presence of cytoplasmic morphologic units consisting of inclusion, elementary and initial bodies may be considered pathognomonic of lymphogranuloma venereum. However, failure to demonstrate these bodies, which appear purplish red with Giemsa stain, does not preclude an active lymphogranulomatous process; for in some instances the demonstration of the inclusions may be somewhat fortuitous, depending on the stage of the infection and the portions of the lesions which are studied microscopically.

With these qualifications in mind, the following observations were made on touch preparations and smears. Smears for inclusion studies came from aspiration material, tissues of buboes and biopsy specimens taken from subacute or chronic infections in cases of rectal disease. Eleven cases were observed, and in each

TABLE 1.—*Effect of Aureomycin on Eight Patients with Lymphogranulomatous Buboes*

Case No.	Size of Bubo on Admission, Before Treatment, Cm.	Microscopic Observations* (Giemsa Stain) Before Treatment	Size of Bubo After Four Days' Treatment, Cm.	Microscopic Observations (Giemsa Stain) After Treatment of Bubo
1	4 by 7	.....	2 by 2	Aspiration bacteriologically sterile
2	5 by 3	Numerous elementary bodies with occasional initial bodies	1.5 by 3	48 hr.: occasional elementary and initial bodies; 1 week later: no inclusion or elementary bodies; aspiration bacteriologically sterile
3	2.5 by 4	.....	Not palpable	.....
4	1.5 by 1.5 Numerous nodes	.....	0.6 by 0.6	Aspiration bacteriologically sterile
5	3.5 by 2.5	As in case 2	2 by 2	As in case 2
6	3 by 0.5	.....	2 by 2	Aspiration bacteriologically sterile
7	5 by 5	As in case 2	4 by 4	As in case 2
8	7 by 5	.....	5 by 4	As in case 2

* In cases 1, 2, 4, 5 and 6 the remnants of the nodes were excised and studied histopathologically; the general pathologic appearance was compatible with lymphogranuloma venereum.

instance a series of specimens was taken. In the cases of bubo, preparations were made before, during and after treatment. Of eight Giemsa-stained preparations studied microscopically, three were seen to contain various morphologic units associated with this virus disease (table 1). The three specimens with positive reactions came from the eight buboes. In 1 instance (case 2) numerous elementary bodies, with an occasional initial body, were noted both in inclusion formation and lying free in the cytoplasm. In this specimen taken from the acute lesion the day of the patient's admission to the hospital, the elementary bodies appeared uniform and took the stain well. Within forty-eight hours after the beginning of treatment a specimen taken from the same bubo revealed only occasional elementary and initial bodies and both units appeared pleomorphic and stained poorly. A third specimen, taken from the same site a week after treatment had been started, contained no inclusion or elementary bodies. While this observation may not be independently significant, it is worthy of note, in view of the patient's rapid clinical improvement. In two other buboes (cases 5 and 7) the described experience was repeated with serial specimens.

Proctitis Due to Lymphogranuloma Venereum.—There were 3 cases of proctitis due to lymphogranuloma venereum in this group, 2 women and 1 man, whose

ages were, respectively, 22, 25 and 27 years. Presenting symptoms were rectal pain, discharge which had been present for three weeks, one year and two years, respectively. Two patients had rectal bleeding. All 3 patients had no associated lesion or other manifestation of this disease. Results of physical examination were essentially negative except for the local pathologic condition. Each patient showed profuse purulent foul-smelling rectal discharge with rectal tenderness on examination. In 1 case there was blood on the examining finger. Proctoscopic examination in all 3 cases revealed a granular mucosa with areas of yellowish exudate. In 1 case the granular area bled very easily. Biopsy in 2 cases showed tissue with acute inflammatory reactions.

Benign Lymphogranulomatous Rectal Stricture.—In this group 14 patients were studied, 13 women and 1 man. Five of these patients had previously had a colostomy for obstruction; 1 patient had a retrovaginal fistula. The ages of the women ranged from 28 years to 57 years, and the man was 27 years. All the cases had been studied previously, and biopsy showed the usual pathologic observations. The duration of the lesions varied from two years to twenty-six years, the average being nine and two-tenths years. There were no significant associated diseases in this group.

TABLE 2.—*Effect of Aureomycin on Rectal Strictures Due to Lymphogranuloma Venereum*

Case No.	Duration (Yr.)	Days on Service	Dosage: Mg. per Day	Dosage: No. Days	Rectal Pathologic Condition on Admission	Clinical Condition After Start of Treatment	Condition on Discharge
12	16	37	10	21	Stricture did not admit finger tip; colostomy; pain and discharge from rectum	No rectal discharge or pain on eleventh day	Stricture admitted finger tip; no pain or discharge; smooth rectal mucosa
13	16	27	10	21	Stricture did not admit finger tip; pain and profuse discharge; perirectal tenderness; colostomy	No perirectal tenderness or discharge on eighth day	Slight rectal discharge; no perirectal pain; stricture unchanged
14	10	37	10	21	Stricture did not admit finger tip; rectal discharge	No rectal pain and defecation easy (first time in ten years) on eighth day	Stricture softer; admitted finger tip; diameter of stool double since treatment
15	26	50	20	50	Stricture did not admit finger tip; profuse rectal discharge; severe rectal pain	Pain and discharge slight on seventh day	No rectal pain or discharge; no change in size of stricture
16	2	44	20	28	Stricture did not admit finger tip; stricture interrupted by recto-vaginal fistula 2 cm. diameter	By the sixteenth day there had been no gas or feces per vaginam for 48 hr.	Rectal and vaginal observations unchanged; no gas or feces per vaginam as on admission.
17	5	32	20	31	Stricture did not admit finger tip; decided decrease in stool diameter, 1 to 1.5 cm.	Stool diameter increased, subjectively improved on twelfth day	Diameter of stool double since treatment
18	7	13	20	8	Stricture did not admit finger tip; decrease in diameter of stool	No change in stricture on fourth day	Diameter of stool increased; no changes in rectal observations
19	4	31	20	31	Stricture did not admit finger tip; bleeding and pain; discharge	No rectal bleeding on the fourth day	Diameter of stool doubled since treatment; no rectal bleeding or pain
20	2	25	20	25	Stricture did not admit finger tip; profuse purulent discharge from rectum; rectal pain; colostomy	Rectal discharge reduced at least 50 per cent by the second day	Stricture unchanged; no rectal bleeding or pain; no discharge
21	2	16	20	16	Stricture admitted index finger; band 0.5 cm. wide in stricture; pain and bleeding on defecation	Diameter of stool greatly enlarged by the seventh day	Stricture not present; no rectal pain or bleeding
22	10	30	20	16	Stricture did not admit finger tip; rectal discharge; diameter of stool diminished	Diameter of stool doubled by the sixteenth day	No change in stricture; no rectal discharge or pain; stools doubled in diameter
23*	6	11	20	10	Stricture admitted finger tip; colostomy; profuse purulent discharge	.....	No change in stricture; only slight rectal discharge
24	10	12	20	11	Stricture did not admit finger tip; decrease in size of stool	Fifth day drug administration: increased size of stool by 50% day	Stricture unchanged; stools doubled in diameter
25	10	14	20	12	Stricture did not admit finger tip; decrease in diameter of stool	Moderate increase in stool diameter by sixth day	No change in rectal stricture; stool diameter doubled

* The patient went home against advice after nine days of treatment.

Reaction to Frei tests were positive in all cases of lymphogranuloma proctitis. Complement fixation tests for lymphogranuloma venereum were 4 plus in dilution of 1:40 in 2 cases. In the third case this test was not done, because of a shortage of sheep cells. Results in all other laboratory studies were observed to be within normal limits throughout the study.

Two patients had eosinophilia; in 1 patient there were 7 per cent and in the other patient 4 per cent eosinophils after treatment. Two patients had leukocytosis which disappeared while the patients were under treatment. Each of these patients was given a daily intramuscular injection of 20 mg. of aureomycin. The total doses given were 80 mg., 200 and 220 mg.

Clinically these patients showed decided improvement. In 2 cases, after four days of treatment, tenderness and discharge disappeared; in the third case, rectal bleeding disappeared after the eighth day of treatment. Proctoscopic examinations at the end of treatment in the 3 cases revealed no abnormalities of the rectal mucosa. One patient, readmitted seventeen days later, complained of rectal discharge, which was considered either a reinfection or a recurrence. After a second period of treatment, with a total dose of 60 mg. of aureomycin, the discharge disappeared. An examination ten days later showed no recurrence.

History on admission showed that 5 patients complained of rectal pain, 2 had rectal bleeding and 7 had rectal discharge. Four patients who did not have a colostomy stated that the diameter of the stool was decreased. One patient complained of passage of gas and feces *per vaginam*.

Physical examination on transfer to this service for study showed, on rectal examination, 5 cases with rectal tenderness, 7 cases with rectal discharge and 2 with blood on the examining finger. The strictures were so advanced, that with the exception of 2 cases, not even the tip of the finger could be admitted into the rectum at the time of admission.

All patients studied had negative Kahn reactions and positive reactions to Frei tests. The result of the complement fixation test for lymphogranuloma venereum in 10 cases was 4 plus in 1:40 dilution, and in 1 case it was 3 plus in 1:5 dilution. Three patients were not tested.

The patients in this group received daily intramuscular injections of aureomycin in amounts of 10 or 20 mg.. The total dose ranged from 160 mg. to 1.0 Gm.

Clinical Course.—As may be noted from table 2, in this group with chronic infections of long duration, the response to antibiotic therapy was gratifying. On the second day of treatment, 1 patient reported considerable decrease in the rectal discharge, while another showed complete cessation of rectal discharge and bleeding by the fourth day of treatment. Five patients showed increase in diameter of stools on the fifth, sixth, seventh, twelfth and fifteenth days of treatment, respectively. Four patients reported decrease in rectal pain and discharge on the seventh, eighth and eleventh days of treatment, respectively. The patient with the rectovaginal fistula had no further passage of feces or gas *per vaginam* after the sixteenth day of treatment.

Examination during and at the end of treatment in 11 cases showed no change in the rectal stricture. One patient that had previously exhibited a small 0.5 cm. band showed no evidence of the band following treatment. Two strictures had become softer and admitted the tip of the examining finger.

Six patients showed stools twice their previous diameter, and 2 patients showed a slight increase in the diameter of stools.

Two patients with rectal bleeding had no bleeding at the end of treatment. Six patients with rectal discharge had no discharge at the end of treatment, and there was decided reduction in 2 cases.

In the 6 patients with rectal pain, all rectal tenderness had disappeared while they were under treatment.

The Anemic Factor.—Since the present study constitutes the first use[4] of aureomycin in human beings, every effort was made to follow the various body systems in each person under treatment. Within a short time after the investigation had been started, anemia was noted in patients receiving aureomycin. Further study revealed the following facts.

In the early cases, the antibiotic was dissolved in a special diluent designed to maintain a low p_H, which was considered desirable. Anemia developed in all patients who received injections with this material (table 3). However, when the special diluent was replaced by isotonic sodium chloride solution the anemia either did not occur at all or, if present, was much less apparent and made its appearance more slowly than formerly. In all instances, even with the use of the special diluent, when a folic acid-iron compound ("folvron") was administered simultaneously with the aureomycin, no anemia was noted.[5]

A critical hematologic evaluation of the anemia made it clear that we were dealing with a simple hypochromic condition of the peripheral blood. That the hemopoietic system was not injured was apparent from the results of bone marrow studies and from the course of the anemia. It should also be noted that blood chemical values were normal in all cases; tests of hepatic function (made in 13 cases) revealed no abnormalities. The urine was consistently normal in all cases throughout the study. Results of tests of renal function (3 cases) were normal. Hematocrit values (20 cases) were normal. The only positive observation was eosinophilia in 18 cases, with the level of eosinophils ranging from 4 to 19 per cent during treatment.

In general, it may be said of aureomycin suspended in isotonic sodium chloride solution that the anemic factor, when it functioned, produced mild easily rectified hypochromia of the peripheral blood. In the absence of apparent toxic effects on any other body system and in the presence of the potent antibiotic activity of aureomycin, the anemia was considered sufficiently minor to warrant continued use of the substance under investigation.

Aureomycin Blood Levels.—Since the schedule of treatment in this report consisted of very small amounts of aureomycin in proportion to body weight, i. e., 10 or 20 mg. daily in adults weighing 50 to 70 Kg., it was of interest to determine (*a*) whether any of the antibiotic was in the blood stream and (*b*) if present in circulating blood, how long the antibiotic remained there.

TABLE 3.—*Effect of Aureomycin on Peripheral Blood*

			Folic Acid-Iron Compound Given		Red Blood Cell and Hemoglobin Values		
	Aureomycin Dissolved in		Same Time as Aureomycin	After Aureomycin Therapy		Interval Values (Days After Aureomycin Therapy Started)	At Time of Discharge from Hospital
Patient	Special Diluent	0.85% NaCl		Was Stopped	At Start Aureomycin Therapy		
12	X	..	..	X	4,420,000 95%	2,850,000 (21 days)	3,800,000 70%
13	X	..	..	X	4,130,000 90%	2,500,000 55% 21 days	4,300,000 69%
14	X	..	..	X	4,400,000 97%	3,150,000 69% 21 days	4,750,000 67%
15	X	..	X	..	3,450,000 72%	4,240,000 85% 21 days	4,300,000 63%
16	X	..	X	..	3,950,000 84%	4,750,000 21 days 90%	4,300,000 79%
17	X	..	X	..	3,910,000 76%	4,600,000 90% 21 days	5,000,000 88%
18*	X	..	X	..	3,940,000 77%	.....	3,850,000 81%
19	..	X	X	..	3,650,000 72%	4,000,000 80% 20 days	4,430,000 72%
20	X	..	X	..	5,150,000 90%	4,870,000 84% 7 days	4,000,000 84%
21	X	..	X	..	3,950,000 65%	3,740,000 65% 7 days	3,750,000 69%
22	X	..	X	..	4,350,000 78%	4,300,000 88% 9 days	4,870,000 77%
23	..	X†	..	..	4,000,000 90%	4,150,000 84% 6 days	4,350,000 87%
24	..	X†	..	..	4,100,000 70%	.....	4,070,000 71%
25	..	X†	..	..	3,400,000 79%	4,330,000 82% 2 days	3,900,000 81%

* Discharged eight days after the start of aureomycin therapy.
† No folic acid-iron compound given at any time.

The technic for estimating the presence of aureomycin in the circulating blood is similar to the inhibition tests used with streptomycin. Details of this test will be published elsewhere.

For present purposes it will be sufficient to describe the manner in which blood samples were collected and to state the results of the blood analyses which were carried out at the Lederle Laboratories.

In accordance with instructions, all blood samples were drawn in amounts of about 15 cc. into rubber-stoppered sterile test tubes. As soon as possible, each tube was quickly frozen by immersion into a mixture of equal parts of methyl alcohol and acetone which contained solid carbon dioxide. The frozen blood was then stored in a refrigerator (solid carbon dioxide) until tested.

In this manner, blood was collected from 7 patients (cases 17, 22, 23, 5, 6, 7 and 10) receiving 20 mg. of aureomycin once daily. In the case of 3 patients, blood was taken at two, six and ten hour intervals after

4. This paper was submitted for publication on May 4, 1948.
5. Since this study was presented for publication, numerous patients suffering with lymphogranuloma venereum and other diseases have been treated with aureomycin. It can now be definitely stated that the anemic factor seen in this first study represented an effect due to the special diluent and not to the antibiotic.

injection of aureomycin. In the remaining 4 cases, the blood samples were drawn just before injection of the antibiotic and two, six and ten hours thereafter.

The blood values representing circulating aureomycin in specimens described were not considered significant.[6] It is to be noted that the present schedule of treatment represented the first tentative approach to therapy; consequently, very small amounts of aureomycin were used and the amount of circulating antibiotic in the blood was not accurately demonstrable by present methods of assay.

SUMMARY

A preliminary study of 25 patients with lymphogranuloma venereum treated with aureomycin, a new antibiotic, is reported. Eight patients with buboes were treated and showed a decided reduction in size of the node at the end of four days of treatment. In 3 instances, on admission of the patients, smears from aspiration of the bubo revealed inclusion and elementary bodies which appeared uniform and took the stain well. Within forty-eight hours after the start of treatment, specimens from the same buboes revealed only occasional elementary and inclusion bodies and both units appeared pleomorphic and stained poorly. One week after treatment, no elementary or inclusion bodies were seen.

Three patients with proctitis were treated and showed decided improvement, in 2 instances after four days and in the third case after eight days. Proctoscopic examination at the end of treatment showed normal rectal mucosa. Fourteen patients with benign rectal stricture due to lymphogranuloma venereum were studied and showed no gross pathologic change in the fibrous rectal stricture, although there was decided decrease in rectal pain, discharge and bleeding. There was an increase in the diameter of the stool.

CONCLUSION

On the basis of our past experience, we believe that in 25 cases of lymphogranuloma at this hospital there were multiple strains of the virus. There is, therefore, the possibility that the effective antibiotic activity of aureomycin is not limited to a single strain.

Aureomycin, a new antibiotic, with apparent virucidal properties, has been used in human beings for the first time. The clinical results in the three types of lymphogranuloma venereum discussed in this paper showed such results as to warrant further extensive research and clinical trial of the antibiotic.

6. Dornbush, A.: Personal communication to the authors.

GENERAL PRACTITIONERS SESSION

CARCINOMA OF THE PROSTATE GLAND

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Carcinoma of the prostate gland is an insidious and deadly disease of slowly increasing frequency. While there were only 83 cases discussed in the literature up to 1899, by 1935 Rich had observed the condition in 14 per cent of autopsies on men, and Moore expressed the belief that he could recognize it in 21 per cent of men past 40. By 1941 Baron and Angrist had claimed that they had observed occult forms in 46 per cent of 50 men past 50 years of age in consecutive autopsies. Using these figures, and assuming that there are 17,000,000 men past 50 in the United States, Hinman has estimated that there must be between 3,000,000 and 8,000,000 cases in this country at any one time. Carcinoma of the prostate gland is listed as the cause of 15,000 to 20,000 deaths in the United States each year (Jewett). To it Huggins attributed 5 per cent of all deaths in men past 50.

This evident increase results from several causes, the principal one being increasing longevity. Life expectancy at birth among the industrial policyholders of the Metropolitan Life Insurance Company rose from 46.6 years in 1911 to almost 67 in 1947. The net result is that two or three times as many men live past the age of 65 as in 1911; this is sufficient to account for the growing numbers of patients who are seen with prostatic cancer. Add to this the fact that education has improved both the physician's ability to recognize the disease and the patient's willingness to consult the physician, and it is unnecessary to postulate a heightened individual susceptibility to cancer.

There is still room for improvement in diagnostic accuracy, because most carcinomas of the prostate gland are discovered only after they have extended locally or metastasized, that is, too late for cure. Thus, Barringer observed that in only 4.5 per cent of 351 cases was the condition localized within the gland at the time of diagnosis, and Young regarded only 3.4 per cent of 1,000 cases as suitable for curative operation.

Late recognition of the disease is due to an unfortunate combination of circumstances. Moore stated that three fourths of prostatic carcinomas arise in the posterior lamella of the gland. Hinman expressed the belief that a smaller percentage arise there but that most of them do begin in the periphery of the gland. In either case, the majority start at a distance from the urethral lumen and grow slowly, so that the first symptom, usually that of obstruction to urination, appears late in the course of the disorder. Unluckily, these symptoms are identical with those of benign hypertrophy, which most elderly men regard as normal accompaniments of aging. All these facts conspire to send the patient to the physician after local extension or metastasis has occurred. Moreover, early or small cancers may be surrounded or covered by layers of benign hypertrophy and so escape detection. Thus, urologists are confronted by the hard fact that at least 95 per cent of patients have inoperable or unrecognizable lesions, as far as cure is concerned, when they are first seen. While this can be remedied to a considerable extent by making rectal examination part of every routine physical examination (as it should be for other reasons), it has led most urologists to take a dim view of attempts to cure carcinoma of the prostate gland. Thus, both the profession in general and the urologist need more education, if they are to discharge their obligations to these patients.

Since, in existing circumstances, most patients require palliative treatment and since this is bound up with endocrine relationships, these will be reviewed.

It has been firmly established that normal development and maintenance of the prostate require male sex hormone from normal testes, which elaborate it under

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the influence of gonadotropins secreted by the anterior lobe of the hypophysis. Castration causes simple atrophy of the normal (not the hypertrophied) prostate and hyperplasia and increased secretory activity of the anterior pituitary. Linked with the endocrine control of the prostate are the phosphatases, enzymes which split phosphoric acid from its esters and which are important in the formation and destruction of bone. The alkaline phosphatases are concerned with many diseases of bone, but the acid phosphatases, while occurring in organs other than the prostate, are of clinical importance only in carcinoma of the prostate. The mature normal prostate has a higher concentration of acid phosphatase than any other organ in the body (Kutscher and Wolbergs). It is elaborated by the acinar epithelium (Gomori) and is abundant in its secretion (Dmochowski). It is present in high concentration in most carcinomas of the prostate and in their metastases (Gutmans and Sproul) and is present in increased concentration in the blood serum of 85 per cent of patients with carcinoma of the prostate which has metastasized to bone (Gutman, Barringer and Woodard, Huggins).

Contemplation of these facts apparently led Huggins in 1939 and 1940 to castrate 20 men with prostatic cancer which had metastasized to bone, on the assumption that, since the normal and the cancerous prostatic cell behave alike with respect to the formation of phosphatase, they might respond alike to castration. Seventy per cent responded favorably, with relief of pain, gain in weight, regression in the local and metastatic lesions and a fall in the acid phosphatase level of the serum. Similar effects followed use of estrogens without castration, and prompt relapse followed administration of male hormone. Spontaneous relapse occurred in most patients after relief varying from a few months to several years and was thought to result from stimulation, by the hyperactive "castrate" anterior pituitary, of the adrenals, which formed androgenic substances. This has not been proved.

Huggins' brilliant study is the basis for most of the effective palliative therapy now in use.

DIAGNOSIS

The history is not helpful unless metastasis to the pelvic bones or local extension of the tumor into pelvic nerve trunks has produced a troublesome sacral backache or pain simulating sciatica. The usual presenting complaint is difficult urination, with nocturia.

The diagnosis depends primarily on recognizing stony induration. At first there is a discrete slightly mobile nodule. Later the whole gland is hard, nodular and fixed by periprostatic extension.

Prostatic tuberculosis may simulate carcinoma, but is ordinarily differentiated by the younger age of the patient, by the story of vesical irritation and urgency without obstruction and by the presence in the urine of pus and tubercle bacilli, with a sterile culture.

The prostatic calculi which do not produce the characteristic crepitus, and which may coexist with carcinoma, are identified by roentgenogram, which will also show metastases to the pelvis when present. Early, there are isolated circumscribed areas of increased density, in which the bony trabeculae are lost; later, these small metastases may coalesce to involve large areas or even whole bones (osteoblastic metastases). In exceptional instances small patches of bone simply disappear (osteoclastic metastases). Confusion is likely to arise chiefly with Paget's disease, in which the trabeculae are increased in size and density, although there may be a patchy appearance that makes differentiation difficult.

It is here that phosphatase determinations are most helpful. In 85 per cent of metastases to bone from prostatic carcinoma the acid phosphatase will be elevated. Huggins regarded a level between 4 and 10 units (King-Armstrong) as suggestive and levels above 10 units as diagnostic. The alkaline phosphatase is also elevated in metastases from the prostate, but in Paget's disease only the alkaline phosphatase is above the normal level of 12.5 units.

Estrogens may be given to clarify the diagnosis. They are useful when observations based on palpation are inconclusive, particularly if local fixation is present and the phosphatase levels are normal; if the roentgenogram shows lesions of uncertain character or even if the prostatic lesion is obviously localized but the patient is a poor surgical risk, one may then give an estrogen in adequate doses for six to eight weeks, at which time definite regression of the local lesion confirms the diagnosis. If it remains stationary or progresses, it may be noncancerous in the first instance or refractory to estrogens in the second. A metastasis to bone which was only suggestive in appearance originally may, after six to eight weeks of treatment, appear larger, denser and more sharply marginated, even if it is destined to disappear later. Failure to change indicates either its nonmalignant character or refractoriness to estrogens.

When the suspected prostatic lesion is discrete and slightly mobile, when there is no evidence of metastasis and when the patient is in good condition, the question of radical perineal prostatectomy arises. Biopsy by aspiration or with the Silverman needle or some punch, such as that of Lowsley, has many advocates but, while adequate in larger lesions, has proved inadequate in my hands because of the difficulty in securing tissue from a small area. My own preference is for perineal exposure of the prostate. If the suspected area is not typical of carcinoma on direct inspection and palpation, it can be excised with surgical diathermy for fast frozen section; if it is typical or if results of biopsy are positive, one should proceed at once with radical removal of the gland.

In some instances Colston has observed that a localized nodule of carcinoma which is adherent to adjacent tissues will regress sufficiently with treatment with estrogens to permit successful radical removal.

While radical perineal prostatectomy is the only method which has yielded bona fide cures in prostatic cancer (56 per cent of five year symptom free survivals by Young and by Colston), many objections to it can be cited, although one does not encounter them in connection with other visceral cancers. The low rate of operability can be improved by a concerted effort. Colston has reported an operability rate of 20 per cent in recent years; Jewett has reported a mortality rate of 3 per cent in patients under 70, and a rate of 10 per cent for men over 70 still compares favorably with that for resections of the stomach or large intestine in similar circumstances. While Kahler has claimed that perineural infiltration outside the prostate is almost always demonstrable, even with small lesions, both Hinman and Young have reported cures as long as seventeen years after operation, which seems to nullify Kahler's claim. The risk of urinary incontinence is not inconsiderable, but can often be corrected; when

the stakes are considered, it does not seem a valid contraindication to the operation. To repeat, it is the only method which has cured any patients.

It should be mentioned that neither the suprapubic nor the retropubic approach gives as good exposure as does the perineal, particularly at the apex of the prostate and the bases of the seminal vesicles.

PALLIATIVE TREATMENT

The employment of palliative measures presupposes that the local lesion has extended or metastasized, that the patient's general condition prevents operation or that stiff hips make the perineal exposure impossible.

Nesbit, Herger and Sauer and others have pointed out that the good effects of endocrine therapy will last only for a limited period (varying from a few months to several years) in the individual patient. This makes it desirable to withhold such treatment until the appearance of pain, for which it is most useful. Its use as a diagnostic measure or in an attempt to make an inoperable lesion operable constitutes a valid exception. For the same reason, it may be preferable to administer estrogens intermittently rather than continuously, stopping the use of them after the symptoms are controlled and restarting when careful follow-up gives evidence of relapse.

Therefore, a patient who has an inoperable carcinoma with few or no symptoms should merely be kept under observation until treatment is demanded by the symptoms and not merely by the knowledge that a cancer is present.

Troublesome obstruction to urination is easily corrected by transurethral resection.

Pain from local extension or metastasis is best treated with endocrine methods. There is no conclusive evidence that castration is superior to estrogens, and I prefer to reserve it for uncooperative or forgetful patients, for those whose severe pain demands prompt relief and for those in whom estrogens are or have become ineffective or impossible to use because of side effects. Huggins, on the other hand, expressed preference for castration, on the grounds that estrogens are less effective, cause soreness in the breasts in many patients and are known to be capable of carcinogenesis. He used the estrogens to combat the hot flashes which follow castration, when operation is refused, as a diagnostic measure and for relapse after castration.

Many estrogens can be used, but diethylstilbestrol and ethinyl estradiol ("estinyl") are usually preferred, because of their known potency and because of their effectiveness when given orally. Both may produce tender enlargements of the breasts, nausea, cutaneous eruptions, hemorrhagic diatheses and mental disturbances, although the incidence of troublesome reactions is low. Diethylstilbestrol is said to cause them more often than does ethinyl estradiol. The dosage recommended varies, in the case of diethylstilbestrol, from 0.5 to 40 and for ethinyl estradiol from 0.15 to 2.5 mg. per day. Either preparation is best given in a single dose at bedtime, in the hope that any nausea will occur at night and will be too mild to awaken the patient. I prefer 5 mg. of diethylstilbestrol daily until symptoms are controlled, followed by a gradual downward revision until a maintenance level is found, after which the treatment is interrupted periodically.

Failure or relapse is treated with doses up to 20 mg. or more daily; if these fail, castration is used. Although prospects of success from castration after the use of estrogens are none too good, an occasional patient will experience striking relief.

The patient who is intolerant of diethylstilbestrol is given a trial of ethinyl estradiol; if this produces side effects, one may implant 40 mg. of alpha estradiol in pellet form subcutaneously at intervals of six to twelve weeks, as recommended by Kearns, before resorting to castration.

Some writers favor various combinations of castration and estrogens, but evidence that this is superior to either one alone is not available.

If pain becomes severe despite these methods or combinations of them, one should not forget the occasional usefulness of roentgen therapy, the subarachnoid injection of alcohol and cordotomy.

Treatment of relapses by irradiation of the pituitary and adrenals, and even by adrenalectomy, has not been successful (Herger and Sauer, Huggins).

RESULTS

Results of palliative therapy are extraordinarily difficult to evaluate concisely, because the best criterion is prolongation of comfortable life, and this is difficult to tabulate. Moreover, no one has yet had time to accumulate any sizeable series of cases followed up for a minimum of five years. In the meantime one can secure some useful information from the death rate of series of patients with and without endocrine therapy for shorter periods.

As a control Nesbit followed up 783 patients treated before 1940 and found that 69.4 per cent had died by the end of the second year after diagnosis. Similar data have been secured from the literature on 569 patients treated by castration, estrogens or both by Vest and Frazier, Greene and Emmett, Nesbit, Herger and Sauer and Huggins. Thirty per cent of these patients had died by the end of the second year, that is, about half the patients who might have died without endocrine therapy were still living. More conclusive data will have to await the passage of time, but Hinman, while recognizing the contribution that the estrogens make to the patient's comfort, expressed doubt that there would be any great net prolongation of life. On the other hand, 5 of Huggins' original 20 patients were living six and one-half to eight years after castration. The series is too small to exclude chance variations, especially since Chwalla observed 2 patients who lived eight and nine years, respectively, after permanent suprapubic cystostomy for prostatic cancer.

Nevertheless, endocrine therapy is affording to many unfortunate old men periods of normal life which simply would not be available without it. Perhaps the most encouraging feature of the whole thing is the prospect that, in the not too distant future, chemical cure of this and other cancers may become a reality.

SUMMARY AND CONCLUSIONS

Carcinoma of the prostate gland has been increasing steadily in frequency during recent years because of increasing longevity with aging of the population.

Prognosis is poor because slow growth leads to late recognition of the disease.

When recognized early, carcinoma of the prostate may be cured in about half the cases.

The chances of cure can be increased only by educating both the patient and the physician.

Palliation by means of endocrine therapy contributes to the comfort of the majority of patients with inoperable lesions.

SPECIAL ARTICLE

CANCER OF KIDNEYS, ADRENALS AND TESTES

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NEW YORK

(Continued from page 362 in The Journal October 3)

CANCER OF THE ADRENAL GLAND

The adrenal gland is actually two glands fused together in development. In the human being these are known as the cortex and the medulla. Each has an essentially different origin, a different type of tissue and a separate function, but they happen to be enclosed in one enveloping capsule and tissue stroma.

Tumors of the adrenal gland are not frequent. When they arise they can be basically classified as follows:

1. Tumors derived from the various layers of connective tissue, blood vessels, lymphatics or nerve structures within the gland are of a type that may occur in any gland. They occur rarely in the adrenal. Tumors of these tissues which have been reported as occurring in the adrenal gland are as follows: fibroma, lipoma, neuroma, neurofibroma, myoma, osteoma, hemangioma, sarcoma, lymphangioma and melanoma.

2. Tumors derived from the medulla are peculiar to that tissue and are of the ectodermal sympathetic nervous system. They may be (1) of the basic nerve cell, a sympathicoblastoma, (2) from the sympathetic ganglion, or a ganglioneuroma, or (3) from the pheochromocytes, a pheochromocytoma or a paraganglioma.

3. Tumors originating from the adrenal cortex are mesodermal glandular tumors and cytologically are hyperplasias, adenomas and carcinomas.

FASCIAL TUMORS OF THE ADRENAL GLAND

Tumors arising from the various layers of connective tissue, the blood vessels, lymphatics and nerve structures of the adrenal gland are extremely rare.

The benign tumors, such as fibroma, lipoma, neuroma, neurofibroma, myoma, osteoma and hemangioma, are usually without symptoms unless they become large enough to cause distress from their size. Often they are discovered by accident in examination, an asymptomatic retroperitoneal mass being found in either flank and the diagnosis being made only on operative removal or at autopsy. When the cancers such as sarcoma, lymphosarcoma or melanoma occur the symptoms are those seen with retroperitoneal cancers, some loss of weight, strength and appetite, a gradual anemia and, depending on the extension of the tumor, epigastric or flank distress. As a rule, studies rule out evidence of changes in the gastro-intestinal tract and in other organs and often an indefinite retroperitoneal mass is discernible by roentgen ray or by abdominal palpation. By surgical exploration and biopsy the diagnosis has been established. Usually surgical removal of these infiltrating tumors has been impossible. High voltage roentgen therapy may benefit in those tumors radiosensitive, as certain of the lymphosarcomas. As yet the effect of the newer therapeutic agents on these rare tumors is unknown. The course in most of these tumors is extension and death. Fortunately they are extremely rare.

TUMORS OF THE ADRENAL MEDULLA

When tumors arise from the adrenal medulla they may be divided clinically into those which do not produce hormones and those which do.

The medulla of the adrenal gland is of the sympathetic nerve system. The primitive nerve cells, the sympathogonia, grow into the hollow of the adrenal cortex so that the cortex extends over and encloses the medulla. The sympathogonia forms two types of cells, one the fibril ganglion cell and the other the secreting endocrine cell.

Sympathogonia

Sympathoblast → Sympathetic ganglion cell

Pheochromoblast → Pheochromocyte (secreting endocrine cell)

Similar ganglion tissue occurs in the retroperitoneal tissues, as the sympathetic ganglions along the aorta and vessels, Zuckerkandl's body, the sacrococcygeal body and the carotid body. Tumors occur in these situations similar to those in the adrenal medulla and may be nonhormonal ganglion cell tumors or hormonal pheochrome cell tumors. The latter have not been reported in the carotid body.

NONHORMONAL TUMORS OF THE ADRENAL MEDULLA

Tumors of the ganglion cell are nonhormonal and occur most often as the extremely malignant immature sympathicoblastomas or less often as the relatively benign neurocytomas of adults.

The immature cell tumors, sympathicoblastomas, occur more frequently in infancy and childhood and the malignancy rates in seriousness with that of the embryomas of Wilms. They occur in either sex, in either adrenal gland or in any of the retroperitoneal sympathetic ganglions. They are seen most often in the first or second years of life and become less frequent as age progresses.

There are usually no symptoms of their presence until profound constitutional changes occur, such as loss of appetite and weakness and anemia, or a tumor mass is accidently discovered in an enlarging abdomen. There may be loss of weight, but this may be offset by the growth of the tumor mass. At other times it is the presence of metastases that attracts attention to the condition. Long ago, Hutchinson [6] called attention to the metastases occurring in the orbit and skull or in the left side of the neck from an original tumor which was later found in the left adrenal gland. Similarly, Pepper [7] reported also finding in infants a tumor of the thorax and the liver occurring secondary to a cancer in the right adrenal gland. In both of these types of tumors, the origin and the cells are the same, adrenal medullary sympathicoblastomas, but the tumors in the right and left glands have different routes of metastases. Most of these cases were unrecognized until metastases had occurred, and this tumor probably in this stage has a complete mortality.

Occasionally such sympathicoblastomas may be recognized before metastases are present. Only by

6. Hutchinson, J.: Left Adrenal Metastasis, Quart. J. Med. 1:33, 1907.
7. Pepper: Am. J. M. Sc. 121:207, 1901.

careful examination of the abdomen, a mass may be found in such infants with a minimum of symptoms. In such, an increase in size of the abdomen may be noticed by the mother before the mass is detected. When found, it usually is in one of the flanks or

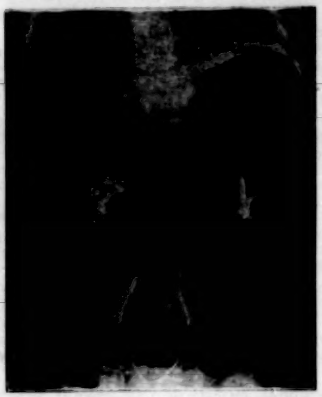

Fig. 5 (R.V.).—A retrograde bilateral pyelogram in an infant girl with a sympathicoblastoma of the left adrenal gland. The tumor mass has pushed the left kidney outward and downward and partially rotated the kidney. The kidney was not involved in the cancer.

sides, and resembles often that seen in Wilms' tumor. It is attached to the posterior part of the peritoneum, usually is soft but may occasionally be hard, projects anteriorly and may be covered by the stomach or intestines. It is without pain or tenderness and may or may not move with inspiration. Excessive handling of the mass is considered to be not without danger of disseminating metastases. When any such mass is present, determination of the origin of the mass is imperative. For this, intravenous or subcutaneous secretory pyelograms have been of great value. Because of the size and age of the infants, secretory pyelograms are, if possible, preferred to retrograde cystoscopy. The diagnosis often is between a renal and an adrenal mass. In the adrenal tumor the films usually show a normal secreting and normal anatomic kidney on that side, often pushed down by the mass above. If so, the greatest odds are that a sympathicoblastoma is present. In a Wilms' tumor of the kidney there is usually diminished secretion on that side due to replacement of renal tissue by tumor growth. There is also distortion and displacement of the renal calyces and of the pelvis by the renal tumor mass. In other words, the adrenal tumor is without the kidney and Wilms' tumor is within. In some cases it may be necessary to do retrograde pyelograms to make a differentiation from a nonsecreting hydronephrosis, or congenital cystic kidney. In some cases, because sympathicoblastomas occasionally invade the kidney, a differential diagnosis is impossible without microscopic section, especially with the retroperitoneal sympathicoblastoma and extrarenal embryoma of Wilms. Surgically it is unnecessary, because the two types require identical therapy. Delineation of these types of large tumors by perirenal insufflation of air has been found unnecessary, may be dangerous and may make removal more difficult.

There are fewer cancers that have a poorer prognosis than the sympathicoblastomas of infancy, mostly because of failure to recognize the disease while the tumors are small and before metastases.

Avoidance of trauma to the tumor and early removal before metastases offer the only correction. Sympathicoblastomas are considered to be among the radioresistant tumors. Wide transverse transperitoneal approach through the upper part of the abdomen is the method of choice. Since most of these tumors grow anteriorly into the abdomen, opening of the retroperitoneal tissue, ligation of all contributing vessels around the tumor and then removal of the tumor are the accepted steps of the procedure. At times the growths may be closely attached to the cava or aorta, but should be removed in spite of attachments and removed intact because, as stated before, in complete removal before metastases lies the sole possibility of relief.

More rarely than the tumors of infancy, similar tumors of more adult cells occur in older age groups, in both children and adults. They occur in the same places, adrenal medulla, retroperitoneal ganglions, Zuckerkandl's, and the coccygeal body, and also in the carotid. Their malignancy is according to the differentiation and activity of the cells. The usual neurocytoma is much more differentiated than the

Fig. 6 (S.F.).—A retrograde pyelogram in a child with a right sympathicoblastoma of the adrenal gland. This shows the large mass above the right kidney pushing the kidney down and rotating it. The kidney was not involved.

sympathicoblastoma and is much less malignant; in fact some of the adult neurocytomas may be considered benign.

Usually they are symptomless; occasionally they may cause pain because of pressure due to their size. Often they are discovered accidently on physical examination. When found, they present a rounded moderate soft smooth mass arising from either flank or from the retroperitoneal tissues of the abdomen. They frequently are movable, attached pos-

teriorly and not tender. Metastatic dissemination is uncommon. For diagnostic purposes, intravenous pyelograms may show no change in renal anatomy or physiology except displacement downward by the tumor. Perirenal insufflation of air may show that they arise from the adrenal fascia area but will not differentiate from any other asymptomatic tumor of the adrenal gland. At times, because of their situation, they cannot be told from asymptomatic tumors of the pancreas or from the various fascial tumors of the area, such as leiomyosarcoma or lymphosarcoma.

The therapy of neurocytoma is surgical removal. This is best by the transverse transperitoneal route through the upper part of the abdomen. Removal may be difficult due to size but usually is not, because they are definitely encapsulated, with no close attachments to organs, and have not the expanded multiple circulatory systems seen with the more malignant carcinomas. Often after complete removal of the tumor there is no recurrence, because of rarity of metastasis.

Cytologically these tumors are graded according to the age of the sympathetic cells and their activity. In extremely young infants the large soft rapidly growing tumor shows sheets of undifferentiated sympathogonia cells with bizarre shapes and many mitoses and with cell disorder. Necrosis in these tumors is frequent. The older more differentiated tumors uniformly show more cells approaching the adult fibril ganglion cell and with more orderly arrangement of the cells and rare mitotic division.

HORMONAL TUMORS OF THE ADRENAL MEDULLA

Tumors of the hormonal pheochrome cells of the adrenal gland are rare but because of interest in the phenomena they are more often diagnosed and reported, and they appear to be more frequent than formerly suspected. The typical syndrome when first described by Labbe and Tinel Doumer [8] was called "paroxysmal hypertension."

The pheochromocytomas are tumors of the secreting endocrine cell of the sympathetic system. They occur in the adrenal medulla most frequently, but also occur in other pheochrome tissue such as the retroperitoneal ganglions, sacrococcygeal body and intrathoracic ganglions. They may be multiple in several ganglions; usually two only have been reported as occurring at a time. The multiplicity has been estimated as to occur in 10 per cent of the cases. MacKeith [9] stated that 9.7 per cent were bilateral and 9 per cent were cancerous.

The secretion from the cells of these tumors causing the syndrome is considered to be an excess production and use of the pressor substance, epinephrine. The symptoms and changes in the metabolism and vascular system are the result of the intermittent or continuous secretion of epinephrine. It has been shown to be in excess during an attack, directly, by Beer, King and Prinzmetal,[10] and, indirectly, by Goldenberg, Snyder and Aranow.[11]

When the tumor occurs the usual symptom complex is seen, which has previously been described as paroxysmal hypertension. This effect has been accepted as a temporary release of an excessive amount of pressor substance into the blood. The reaction of the patient is to this excessive amount of pressor substance. More recently it has been shown by Palmer and Castleman,[12] by Howard and

Fig. 7 (J.L.).—Air insufflation roentgenogram in a case of pheochromocytoma of the left adrenal gland. The area of the right adrenal gland is normal and the wedge-shaped normal gland is visualized. On the left side the ovoid-shaped gland is shown about four to five times the size of a normal adrenal gland.

Barker,[13] by Quinby[14] and others that with continued growth of the tumor a continuous sustained hypertension may follow the intermittent hypertension so that a symptomatic picture may be present that in time may resemble the so-called essential hypertension.

The tumor and its syndrome occur more frequently in young or middle adult life. It may occur in children. It is rare in old age. It has been described in both sexes but is much more frequently seen in women.

The usual symptom complex of paroxysmal hypertension may occur either spontaneously or may be induced. Usually the symptoms are brought about by emotional crises or sudden physical activity. In the same person the symptoms are usually similar each time they occur. They start often with a pronounced beating of the heart, a pounding headache, epigastric distress or pain and often a sense of constriction of the hands and feet. The attack is emotionally disturbing and may be associated with a sense of impending death; it may last for a few minutes to several hours. With the ending of the attack, excessive perspiration occurs, with exhaustion and fatigue, and if the attack lasts long or is severe it may be followed by shock. After the attack there may be cutaneous dilation of the blood vessels of the hands and feet, which are cold, at times blanched, during the attack. Associated with the attack is a definite rise in both systolic and diastolic blood pressure and a subsequent fall to normal or a lower level on its ter-

8. Labbe, M. J., and Tinel Doumer: Suprarenal Tumor, Bull. et mem. Soc. med. d. hop. de Paris 46:982, 1922.
9. MacKeith, R.: Adrenal Sympathetic Syndrome, Brit. Heart J. 6: 1, 1944.
10. Beer, E.; King, F. H., and Prinzmetal, M.: Pheochromocytoma With Demonstration of Pressor Substance in Blood Preoperatively During Hypertensive Crises, Ann. Surg. 106:55, 1937.
11. Goldenberg, M.; Snyder, C. H., and Aranow, H., Jr.: A New Test for Hypertension, J. A. M. A. 128:971, (Dec. 18) 1945.
12. Palmer, R. S., and Castleman, B.: Paraganglioma of Adrenal Gland Simulating Malignant Hypertension, New England J. Med. 219: 793, 1938.
13. Howard, J. E., and Barker, W. H.: Paroxysmal Hypertension, Bull. Johns Hopkins Hosp. 61:371, 1937.
14. Quinby, W. C.: Tr. Am. A. Genito-Urin. Surgeons 36:103, 1943.

mination. Examinations of blood and urine during and for a while after the attack show sugar curves similar to those seen with diabetes mellitus. This is more often seen in adults and older persons and less frequently seen in children. At times death may occur during or after an attack, most often associated with pulmonary edema.

In some cases a more sustained and continuous hypertension may result as the disease progresses, so that the symptoms may be confused with "essential hypertension." When such occurs, vascular changes may result and may remain permanent even though the tumor is removed. These vascular changes may be present in the eye grounds. The type of vascular changes in the eye grounds occurring in the cases in children has been reported by Bruce[15] to be specific to the condition and not seen by him in other hypertensive conditions.

The diagnosis of pheochromocytoma depends on (1) a history of typical attacks and associated clinical findings; (2) evidence in so-called essential hypertension of the symptomatic and clinical findings in the pheochrome syndrome; (3) demonstration in the blood during the attack of a pressor substance as shown by Beer, King and Prinzmetal[16] or, more easily, a significant reduction in the blood pressure by the intravenous introduction of an epinephrine antagonist, such as the benzodioxane series as described by Goldenberg, Snyder and Aranow[17]; (4) precipitation of an attack in the resting stage by an epinephrine-producing stimulus such as histamine, as described by Roth and Kvale,[16] and (5) roentgenographic evidence in a case with the syndrome of the presence of the tumor, without or with perirenal insufflation of air or by renal displacement as shown through the use of films with pyelographic mediums.

A number of metabolic changes have been found with these tumors. Hypermetabolism is of frequent occurrence, and differentiation between hyperthyroidism and pheochromocytoma by symptoms is sometimes difficult. Concomitant swelling of the thyroid with tumor and syndrome has been described by Bauer and Belt.[17] Elevation of the serum potassium and increased urea clearance have been found. The glycosuria present may confuse the diagnosis, but it is usually resistant to the ordinary treatment of diabetes mellitus. The sugar changes, as before stated, are greater in older persons. Hysteria and psychoneurosis may present difficulties in diagnosis.

Recent operative reports show a decided lowering of the mortality in the surgical therapy of these tumors. The only known cure is removal. The use of tribromoethanol in anesthesia induction has usually avoided the precipitation of an attack. Because of their situation and the possibility of multiplicity, the transperitoneal approach has been used most frequently. In the removal of these tumors danger lies in their handling during the operation. Experience has shown that all vessels to and from the tumor should be ligated before the tumor is handled. Handling of the tumor without vascular separation has been shown in some cases to be immediately followed by death, from release of a fatal excess of epinephrine. When the tumor is successfully removed, there is an immediate fall of blood pressure. This at first may require administration of epinephrine but usually shortly afterward returns to normal levels. In some cases the return is slow and accompanied by lethargy. After removal there is usually no mortality and cure results. Cases have occurred in which symptoms have persisted after removal of a tumor. This has usually been due to the presence of another unrecognized tumor, which is another reason for complete transperitoneal examination of the abdomen, because by far most of these tumors are intra-abdominal. Rarely, because of vascular difficulties or vascular attachments, a tumor may be incompletely removed. Not infrequently the persistence of the symptoms is due to functionating metastases. There are no known clinical means for determining whether the lesion is benign or cancerous either before operation or at operation, except by noting extension of the tumor through its capsule and local invasion—the usual extension of these tumors, because death most often intervenes before widespread metastases occur.

These tumors cytologically show excess of pheochrome cells with increase of interstitial stroma and ganglion cells. The hormonal activity of these cells can be determined by biologic assay or by demonstrating the amount of hormonal material in the cells by special stains. Malignancy is determined by the cell structure and by the cell invasion through the stroma and capsule.

TUMORS OF THE ADRENAL CORTEX

Tumors of the adrenal cortex are classified as follows[18]: (1) tumors with no recognizable hormonal changes in the patient; (2) tumors with changes due to hormonal influence on the secondary sex characters (adrenogenital); (3) tumors with changes due to hormonal influence on various metabolic processes (adrenometabolic tumors) (Cushing's syndrome), and (4) tumors with changes due to various hormonal influences, both of the adrenogenital type and the Cushing syndrome of the adrenometabolic type (a mixed syndrome).

Nonhormonal Tumors Of Adrenal Cortex.—The nonhormonal tumors are not infrequent. They have occurred mostly in adults, usually over 30 and more often in the later decades, and have been seen in both sexes. They are usually silent. When recognized, they have usually been present for a considerable time. At first without any symptoms, they may later cause a deep pain in the abdomen or pain in the flank on the side in which the tumor is present. Often they are studied by roentgen examination of the gastrointestinal tract without discovery. Later, with increasing size of the tumor, a mass is found on the affected side. The deep location of the adrenal gland and the slow growth of the tumor and its slowness of invasion of adjacent viscera often allow the tumor to grow extremely large before it is discovered. The pain occurring may be abdominal and in the flank or both and is usually made worse by activity. There are frequently some loss of weight, fatigue and diminution of appetite, and mild anemia may be present. These tumors are not tender. Not infrequently, at

16. Roth, G. M., and Kvale, W. F.: Tentative Test for Diagnosis of Pheochromocytoma, J. Lab. & Clin. Med. 30: 866, 1945.
17. Bauer, J., and Belt, E.: Paroxysmal Hypertension Due to Pheochromocytoma of Right Adrenal Gland, J. Clin. Endocrinol. 7: 30, 1947.

18. Cahill, G. F.: Hormonal Tumors of the Adrenal, Surgery 16: 228, 1944.

the time of the first recognition of the tumor, pulmonary metastases may be demonstrated by thoracic roentgenograms. In others, in spite of the extraordinarily large size of the tumor, no metastases seem to occur.

When examined by roentgen rays, especially with pyelographic studies, these tumors usually show a mass in the flank above the kidney and displacing it downward on that side. At times the tumor may project anterior to the kidney, and its outline may be demonstrated by the shadows of other viscera. If the tumor is small it may be necessary to demonstrate its presence by perirenal insufflation of air. If the tumor is large and freely palpable such a procedure may not be necessary. Some of these tumors have occurred in accessory adrenal glands, either in the prerenal area, where they have been

Fig. 8 (A.M.).—A retrograde pyelogram of a case of a large carcinoma of the left adrenal gland, without any hormonal symptoms. The large dense shadow of the tumor is seen above; it has pushed the kidney down and turned it so that it is visualized as if it were seen with the lower pole anterior and the upper pole posterior.

confused with tumors of the tail of the pancreas, or in the broad ligament of the pelvis, where they have been taken for ovarian or other pelvic tumors. Most of these tumors, although definitely encapsulated, are malignant, and because of their silence and large growth the prognosis is sometimes poor. The tumors are often irregular in shape, may be nodular and may vary within the tumor from dense hard areas to softer areas, often necrotic. They are yellowish and resemble the clear cell hypernephroma of the kidney in gross appearance. On microscopic section they show cells of bizarre shapes and sizes and arrangements. In some of these tumors the cells are of tremendous size; the largest cells occurring in the human body have been seen in these tumors. Only rarely are cells with vacuoles containing steroids seen in this type.

The accepted therapy is complete removal of these tumors, usually through a transverse or oblique anterior transperitoneal approach. After the posterior peritoneum fascial planes are opened the viscera anterior to the tumor are usually displaced downward and inward, and after the vessels to the tumor are ligated they usually are removed easily in spite of their huge size, because of their encapsulation. Recovery from removal is the rule, and as numbers of these patients have apparently no metastases, freedom from extension or recurrence often occurs.

Hormonal Tumors of Adrenal Cortex.—Tumors with

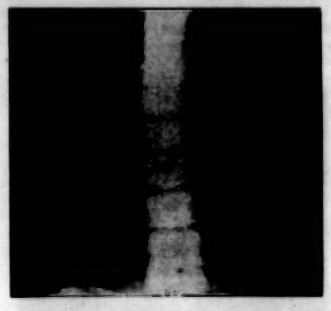

Fig. 9 (S.S.).—An air insufflation roentgenogram in a case of carcinoma of the left adrenal gland in a male without hormonal symptoms. The rounded denser shadow shows the adrenal gland growing down in front of the kidney, which can be visualized through the tumor because of the air, which also surrounds the kidney within Gerota's fascia.

changes due to hormonal influence on the secondary sex characters are divided into: *(a)* changes due to excess androgens (1) in a girl toward adult masculinity, (2) in a boy toward adult masculinity; *(b)* changes due to excess estrogens (1) in a man toward femininity.

Tumors with Symptoms Due to Excess Androgens: In a girl toward adult masculinity. When the disease occurs at birth or in early childhood the symptoms have been described as pseudohermaphroditism. The changes of male character due to excess hormonal secretion are not infrequent in girls, but tumor as a cause is rare. The most frequent cause of the changes is bilateral adrenal hypertrophy. With the exception of survival time there is often no difference between the symptoms of bilateral adrenal hypertrophy and unilateral tumor. Both begin with hypertrophy of the clitoris, appearance of hair on the genitals, excessive bodily growth for a while, increase in musculature, deepening of voice, accelerated epiphysial and dental development and often a higher mental aptitude for their age. Acne is often present. There is often a decrease in size of the vagina and other female characters. The children are at times aggressive and combative like boys. Some, on the other hand, acquire a shut-in personality.

When the symptoms are due to tumor, the tumor may be adenoma or carcinoma. The tumors are most often unilateral, and are well shown with roentgenograms taken after insufflation of air. The urine contains androgens far in excess of their age. These androgens are now registered by the amount of 17-ketosteroids excreted in the urine. Very high excretion of 17-ketosteroids has been described as due only to carcinoma, but recently similar high excretions have occurred with bilateral adrenal hypertrophy.

The older prepuberty girls with the syndrome do not menstruate even though the period of puberty has been reached. Rarely a fleeting menstruation has been reported. With the older children a more general hirsutism is apt to develop on face, lips, chest and back, and acne is usually present. In these children the voice may be surprisingly deep. A rapid transitory growth of the child is often followed by a closure of the epiphyses, and if the child recovers from the disease, relative shortness in stature may be the result.

Fig. 10 (M.H.).—An air insufflation roentgenogram of a girl with male puberty symptoms, due to a large cancer of the right adrenal gland. The air infiltrated around the left adrenal gland but poorly around the right, which is shown as the dense mass round in shape above the area of the right kidney.

Tumors in a woman causing changes toward adult masculinity. In the woman after puberty and before menopause there occurs what is called the adrenogenital syndrome. According to Wintersteiner[19] this in its broadest sense comprises all conditions in which the abnormal changes in the sexual sphere are referable to organic or functional disturbances in the adrenal cortex. In these women it consists of the appearance of male secondary sex characteristics and the suppression of female characteristics and function. When the syndrome becomes established after puberty or later in life, the first change noted is the appearance of hair on face and body of male type; this, called hirsutism, is followed by irregularity or cessation of the menses, changes in body contour and enlargement of the clitoris. Such syndromes are not infrequent. In many clinics women appear with some or all of the symptoms, seeking a change back to normal. From studies made on these patients, tumor of the adrenal gland is not a frequent cause of the change. Normal anatomic or hypertrophied adrenal glands are usually noted. When tumor does occur, however, the symptoms are clearcut. The hair definitely has an acceleration of growth; when menses cease the cessation is complete. Headaches at the time of menses are frequent with tumor. Acne is present and may be pronounced; clitoral hypertrophy is evident, and the younger the patient the more pronounced is the change. Deepening of the voice, and recession of breasts, labia, uterus and sexual desire often follow. Associated with these changes are the appearance of excess amounts of androgens in the urine. These are now determined by the estimation of the 17-ketosteroids, and with tumor these have been high in these cases, over 100 mg. per liter.

It is in this type of case that the roentgenograms taken after insufflation of air have been most helpful in the diagnosis. The clear fascial planes in these cases allow the air to infiltrate easily and outline the adrenal glands and tumor, if present, extremely clearly.

When tumor is present in these females, both children and adults, surgical removal is indicated. It may be done through the flank or preferably transperitoneally. Removal of these tumors is not difficult and is usually free from complications of adrenal failure. Recovery is rapid and the regression of the male characteristics occurs with the restoration of those of the female. Menses often return in a month or so and the excess hair sheds most profusely at the menstrual periods. Most of these tumors have been adenoma or adenocarcinomas and the cells have acidofilic granules in the cytoplasm, and some have steroid vacuoles. The excess of granular cell cytoplasm has given the name of "granular cell tumors" to this group.

In a boy toward adult masculinity. The usual symptom described in the class has been precocious puberty (pubertas praecox). Precocious puberty by itself is not infrequently seen with many causes. Adrenal tumor is a rare cause, much less frequent than similar tumors in girls.

Fig. 11 (F.H.).—An air insufflation roentgenogram of a boy with precocious male puberty. The round outline of the adrenal tumor is shown between the spleen above and the kidney below. This was a "granular cell" tumor.

When tumor occurs there is an increase in size of penis and scrotum without corresponding increase in size of the testes. Hair appears on the pubis and may appear on the face. The child shows increased growth, muscularity and dentition, and advanced epiphysial changes can be seen roentgenologically. The growth may be of the infant Hercules type. The child is often aggressive and unruly and may show postpubertal changes with masturbation and sometimes ejaculations. There

19. Wintersteiner, O.: Adrenogenital Syndrome, J. A. M. A. 116: 2681, (June 14) 1941.

is a decided increase of androgen output in the urine as shown by the estimation of the 17-ketosteroids.

In these cases the roentgenograms after insufflation of air have again clearly shown the adrenal status, especially presence or absence of a tumor. If a tumor is present, operative removal is indicated. Some of these boys have shown mixed syndromes suggestive of excess of other metabolic hormones besides the androgenic. These syndromes, such as obesity and redness of face with hemoconcentration, would require adrenal substitution therapy during and after removal of the tumor, because such metabolic syndromes are often associated with atrophy of the opposite adrenal gland and substitution therapy may be necessary until the opposite adrenal gland resumes secretion.

Some of the tumors have been adenomas and others adenocarcinomas. Like the tumors in females they have cells with acidofilic granules in large numbers if only the adrenal-sex syndrome is present, but if obesity and other signs of Cushing's type are present there will be found large numbers of foam cells, cells with multiple steroid droplets in the cytoplasm.

When the tumor has been successfully removed in these cases there is a recession of the child's precocious puberty and the child resumes a normal course of life. The fixed changes in the epiphyses do not regress.

Tumors With Symptoms Due To Excess Estrogens.—Tumors with symptoms due to excess estrogens are rare, producing changes in a man toward femininity. The usual symptoms are decrease in size of the penis, enlargement of the breasts and nipples, loss of sexual desire and impotence. The symptoms have been progressive in the few rare cases in which the disease occurred and then with loss of weight, anemia and emaciation; a tumor mass was found in the abdomen as the cause. Levy-Simpson and Joll [20] showed in 1 of these cases that the effect on the patient was the result of excess estrogens elaborated by the adrenal tumor. The excess estrogens disappeared from the urine on the removal of the tumor, with disappearance of the symptoms. After a time the symptoms reappeared with reappearance of excess estrogens in the urine, when multiple metastases appeared in the lungs and liver before death. The few reported cases have been mostly carcinoma of the adrenal gland and all have been fatal. Fortunately, because of the unique syndrome autopsy studies have been thoroughly made in these few cases.

Tumors with Syndrome Due To Hormonal Influences on Various Metabolic Processes: (Cushing's Syndrome) The syndrome which was described by Cushing,[21] who suggested that it might occur with basophilic adenoma of the pituitary, was also recognized by Achard and Thiers [22] in their "diabetes of bearded women." Cushing, however, outlined a clinical picture in either male or female, consisting of a rapid plethoric painful obesity affecting primarily the face, neck and abdomen but usually sparing the extremities, this giving rise to an obesity described as the "buffalo type." The facial changes made the eyes appear small and slitlike, like those of pigs, and the picture is called "moonface." There was acrocyanosis with purplish linear atrophy on the lower part of the abdomen and the thighs. Hirsuties might be present. There was a tendency toward polycythemia and some hypertension, and glycosuria were of frequent occurrence. With the syndrome came muscular weakness and porosis of the bones, causing a cervicodorsal stoop and a shortening of the stature. Amenorrhea was present in the women and impotence in the men. There was a definite susceptibility to infectious processes and to physical stress. Mental changes were present and in some, well developed psychoses occurred. Much discussion has occurred as to the cause of Cushing's syndrome. It has been definitely shown that it may be caused by adrenal tumor and that, if the tumor was removed and the patient survived the acute adrenal depletion following, the syndrome described by Cushing gradually disappeared and the patient returned to normal health.

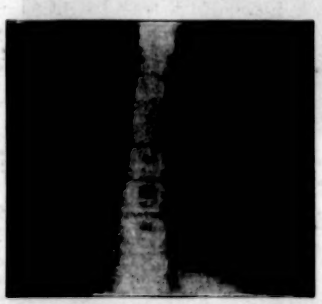

Fig. 12 (H.P.).—An air insufflation roentgenogram of a woman with Cushing's syndrome due to tumor of the right adrenal gland. The ovoid tumor is clearly seen in the outer part of Gerota's fascia above the right kidney. This was a "foam cell" tumor.

Albright [23] from his study stated that the Cushing syndrome is a definite opposite syndrome from the adrenogenital syndrome, the first due to excess production of the S hormone and the latter to excess production of the N hormone. All patients with Cushing's syndrome suffer from an hyperadrenocorticism. The complicated metabolic changes which vary in all patients suffering from the disease make a standard impossible.

The syndrome is most frequently seen in women, less so in men, and it occurs rarely in children. The most frequent adrenal change found associated with the syndrome is bilateral adrenal hypertrophy with microscopic section showing changes known as "foam cell adrenals." Tumor of the adrenal gland occurs as a cause less frequently. The tumors are usually adenomas; rarely is carcinoma found as a cause of true metabolic syndromes. When the syndrome occurs the diagnosis may be made by roentgenograms of the adrenal gland after insufflation of air or by bilateral exploration. Operative removal of these tumors may be followed by acute adrenal deficiency and death if the opposite adrenal

20. Levy-Simpson, S., and Joll, C. A.: Feminization in Male Adult With Carcinoma of Adrenal Cortex, Endocrinology 22:586, 1938.
21. Cushing, H.: Basophil Adenomas of Pituitary Body and Their Clinical Manifestations, Bull. Johns Hopkins Hosp. 50:137, 1932.
22. Achard, C., and Thiers: Le virilisme pilaire et son association a l insuffisance glycolytique: Diabete des femmes a barbe, Bull. Acad. de med. 86:51, 1921.
23. Albright, F.: Cushing's Syndrome, in Harvey Lectures, 1942-1943, Baltimore, Williams & Wilkins Company, 1944, p. 123.

gland is in a nonfunctioning state due to the excess hormones of the tumor. Administration of a potent hormone substance in sufficient amount until the nonfunctioning adrenal gland has resumed its normal role in metabolism is the therapeutic step for correction of the acute addisonian crisis.

Tumors with Changes Due to Hormonal Influence on the Secondary Sex Characters and on Other Metabolic Processes: A clinical case of mixed syndrome is sometimes seen as often as the Cushing type. The most frequent adrenal cause has been bilateral adrenal hypertrophy. It has been caused by tumor, and a high proportion of these tumors have been carcinoma. It occurs more frequently

Fig. 13 (L.F.).—An air insufflation roentgenogram in a case of carcinoma of the right adrenal gland with "mixed" syndrome. The outline of the tumor can be seen above the right kidney. The tumor was globular and compressed tightly against the liver. The cells of this tumor were both granular and foam cells.

in the female in an older age group but has occurred in both male and female children.

When the syndrome occurs in women with carcinoma, the sexual changes are not as great as in Cushing's syndrome. The diagnosis of 3 such cases in the Squier Clinic was made by the symptoms and the roentgenograms after insufflation of air. Operative removal of the tumors in these cases was followed by acute adrenal deficiency. In one of the cases recovery was undoubtedly due to metastases functionating subsequent to removal of the adrenal tumor. In the 3 cases of this group at that clinic, microscopic section showed all to be carcinoma of both cells with granular cytoplasm and with foam cells.

CANCER OF THE TESTIS

Testicular tumors are not infrequently observed in urologic practice. Eighty-two cases were noted in over 27,000 admissions to the Squier Clinic, and Young [24] reported the finding of 25 tumors among 12,000 admissions at the Brady Clinic. Tanner [25] estimated that this type of tumor occurred once in every 2,000 hospital admissions. Hinman [26] reported that it occurred among 0.063 per cent of male patients admitted to the hospital. It made up about 0.57 per cent of all tumors. Dean [27] stated that testicular tumors represent 1.008 per cent of all tumors of both sexes and that 2.09 per cent of all malignant tumors of males were primary in the testis. The right side seems to be slightly more involved than the left. Bilateral involvement occurs, simultaneous or subsequently; the tumors are rare and are more frequent in cryptorchids.

It has been stated, and it appears to be supported by study, that tumor is more frequent in undescended testes than in normal testes. Incidence of tumors in undescended testes varies from 8.4 per cent reported by Higgins and Buchert [28] to 14.29 per cent reported by Dean.

The tumors occur most often in the period of maximum sexual activity. They may occur in infancy, usually as a teratoid, or may occur in old age, more often as a seminoma.

A history of trauma may be elicited in many cases of testicular tumors. The frequency varies from 10 to 30 per cent, according to the author (Cairns,[29] Dean,[27] Smith,[30] Higgins and Buchert [28]). The fact that the testis is an exposed organ and that even trivial injuries are painful and more apt to be remembered by the patient may contribute to the large incidence of trauma that is in the literature.

Over the last forty years there have been many divergent pathologic classifications of testicular tumors. New growths may arise from any type

Fig. 14.—A plain roentgenogram of the abdomen in a case of carcinoma of the left testis and a metastases in the left lumbar glands giving a bulge shadow to the upper part of the edge of the left psoas muscle. A case suitable only for external radiation.

of cell in the testis. Adami [31] best described the testicular cell itself as a tripotent cell which has the power to give rise to every order of cell in the body. Thus tumors may occur from any of the three germinal layers, the epiblast, mesoblast and hypoblast. The majority seems to be of two main types, the seminoma tumor from the seminal cell and those of teratoid or embryonal origin. A classification used by Friedman and Moore [32] may be suggested because it is simple: (1) seminoma (germinoma), (2) embryonal carcinoma, (2a) chorioepithelioma, (3) teratoma and (4) teratocarcinoma. According to Friedman and Moore, over 96 per cent of the 922 tumors of the testis seen by them in

24. Young, H. H., and Davis, D. M.: Young's Practice of Urology. Philadelphia, W. B. Saunders Company, 1926, p. 672.
25. Tanner, C. O.: Tumors of the Testicle with Analysis of One Hundred Original Cases, Surg., Gynec. & Obst. 28:542, 1922.
26. Hinman, F.: The Prognosis and Treatment of Tumors of the Testis, J. Urol. 24:72, 1930.
27. Dean, A. L., Jr.: Teratoid Tumors of the Testis, J. A. M. A. 105:1948, (Dec. 14) 1935.
28. Higgins, C. C., and Buchert, W. I.: Malignant Tumors of the Testicle: Review of Eighty Three Cases, Am. J. Surg. 43:675, 1939.
29. Cairns, H. W. B.: Neoplasms of the Testicle, Lancet 1:542, 1936.
30. Smith, G. G.: Diseases of the Scrotum and Testicle, in Cabot, H.: Modern Urology, ed. 2, Philadelphia, Lea & Febiger, 1936, p. 597.
31. Adami, J. G., and McCrae, J.: Text-Book of Pathology, N. Y., Lea & Febiger, 1914, p. 525.
32. Friedman, E. B., and Moore, R. A.: Tumors of the Testis, Mil. Surgeon 99:572, 1946.

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the Army Institute of Pathology fell into these categories. Whatever classification is used or whatever interpretation is made about testicular tumors it should be understood that pathologists and clinicians agree that for all practical purposes all tumors of the testis are to be regarded as cancerous.

The common tumors of the testicle more often form metastases by way of the lymphatics. The

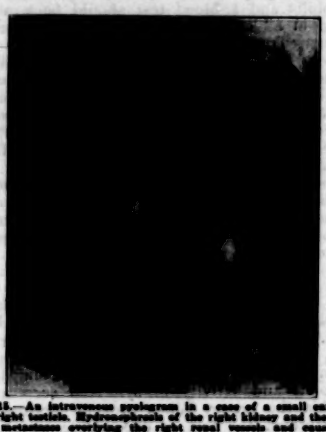

Fig. 15.—An intravenous pyelogram in a case of a small carcinoma of the right testicle. Hydronephrosis of the right kidney and the outline of the metastases overlying the right renal vessels and causing the hydronephrosis may be seen. A case suitable only for external radiation.

teratogenous tumors are thought to metastasize earlier than the seminomas. The metastases of both at times may be early but more often the tumor may be present for a considerable period without metastases. Metastases do occur by way of the blood stream but much less frequently and may give rise to general metastases without involvement of the primary lymphatics.

The primary lymphatics of the testicles drain along with the spermatic vessels, cross the ureter and empty in the lateral lumbar nodes. These lie lateral to, around and in front of the large vessels below the renal vessels. The chain of nodes extends from the common iliac artery to the renal vessels. The secondary lymphatics drain into (1) the primary nodes of the opposite side and (2) nodes behind and between the great vessels above and below the renal veins. Extension from these glands may be to and through the mediastinum and to the supraclavicular group.

Involvement of the lungs may occur by lymphatics or by the blood stream, appearing as round masses, denser than normal lung tissue, and scattered throughout the lungs. Metastases may occur generally in the liver, facial bones, intracranially and in various places. Metastases in many cases must be late because the enlargement of the testis has often been noted for years. Testicular tumors rarely break through their fascial coverings and invade the scrotum. Extension to the scrotum has been seen with exploratory puncture or ill advised incision into the tumor. Only when these unusual fascial invasions occur does one see involvement of the inguinal nodes, or rarely these nodes are involved late by retrograde flow after the retroperitoneal nodes are blocked with tumor infiltration.

Seminomas.—Roughly one third (35 per cent) of the tumors reported by Friedman and Moore were seminomas. This was from a group of patients mostly between 19 and 39 years of age. From all age groups, Cabot and Berkson [32] stated that seminoma occurred in 59 per cent of proved testicular tumors. Similar figures were reported by Geist and Thalhimer,[34] by Herman [35] and by Nash and Leddy.[36] It is of record that seminoma occurs more frequently with increasing age.

These tumors are grossly round or ovoid, elastic, with uniform appearance and heavy to feel. The microscopic appearance is of mostly uniform size rounded monocellular elements with clear cytoplasm. These cells are considered to arise only from the seminal cells. The cells are remarkably uniform and are usually in masses or cords divided by trabeculae of connective tissue. There may be lymphocytic infiltration of this connective tissue, and foci of coagulation necrosis are frequently encountered in these tumors. Occasionally variations of structure occur, so that about 4 per cent of the

Fig. 16.—An intravenous pyelogram in a case of carcinoma of the left testicle, with a large palpable left epigastric mass of metastases that displace the left kidney laterally and obstruct it. This case is suitable only for external radiation.

tumors will have some embryonal carcinomatous tissue. Seminomas usually do not invade or destroy tissue planes or adjacent structures and scrotal invasion is rare.

Embryonal Carcinoma.—Embryonal carcinoma shows considerably more variation in its cell components. The cells are of various shapes, and frequently glandular or papillary structures are present. These tumors are often of undifferentiated cells and appear as solid sheets of anaplastic cells with large and bizarre nuclei. Syncytial cell masses may be seen. Some have frankly teratoid structures, such as the embryo masses of Melicow.[37]

32. Cabot, H., and Berkson, J.: Neoplasms of the Testis: Study of the Results of Orchidectomy With and Without Radiation, New England J. Med. 236:122, 1950.
34. Geist, S. H., and Thalhimer, W.: Histopathology of Carcinoma of the Testicle, Ann. Surg. 66:971, 1917.
35. Herman, L.: The Practice of Urology, Philadelphia, 1930, W. B. Saunders Company.
36. Nash, L. A., and Leddy, E. T.: Seminoma of the Testis, Am. J. Roentgenol. 60:162, 1948.
37. Mellow, H. H.: Embryoma of Testis, J. Urol. 44:833, 1940.

Choriocarcinoma.—Choriocarcinomas have two cellular components and in their arrangement tend to duplicate the placental villi. The two groups are a mass of compact cells with giant multinucleated cells at the borders of these masses. A complete choriocarcinoma is rare. Focal choriocarcinoma occur in about 12 per cent of embryonal carcinomas and teratocarcinomas. Gynecomastia and changes in the endocrine glands occur in cases of choriocarcinoma by itself and in the cases of focal choriocarcinoma.

Teratomas.—Epithelial masses, glands and cysts in association with some undifferentiated tissue and specialized structures such as cartilage or bone make up the usual character of the teratomas. Rarely are teeth and hair present in these tumors. The tissue seen is mostly of differentiated adult type.

Teratocarcinoma.—Teratocarcinomas are a large group of testicular tumors in which differentiated teratoid structures are present with histologically cancerous elements of embryonal carcinomas and choriocarcinomas. Less often will there be semi-nomatous components present.

CLINICAL FEATURES OF TESTICULAR TUMORS

The subjective symptoms of testicular tumors either may be nonexistent or may vary according to the interpretation of the patient. In most cases the presenting sign is enlargement of the testis. Usually the duration of the enlargement may not be known. If the tumor occurs in an undescended testis the first presenting sign may be a mass metastasis. The tumor mass usually is without pain or tenderness. A dragging or uncomfortable feeling is as far as pain goes. Some patients definitely state that the testis feels heavier than it should. At times an associated hydrocele may be present, fluid from which is bloody. Some complain of an abdominal mass in addition to scrotal enlargement. Others may have fixed pain in the back and unrecognized testicular change. Enlargement of the breasts may occur without recognition of change in scrotal contents. All in all there is no definite group of symptoms, most patients coming for consultation because of simple enlargement of the scrotum.

DIAGNOSIS

All enlargements of the scrotum form a group among which tumor of the testis must be recognized. Tumor of the testis involves the testis only. It may be smooth and it may be irregular and nodular. It usually has some areas of rather decided hardness and is much heavier than fluid or normal tissue of the same size. The heaviness of testicular tumor is a characteristic of this particular neoplasm. It is movable in the scrotum, rarely fixing itself to its coverings or the scrotum. The mass is rarely tender, has no feeling of heat and shows no change in the color of the skin. Enlargement of the scrotal veins may be present. The vas is usually normal. Puncture biopsy for diagnosis is not recommended in these tumors.

Tumor of the testis must be differentiated from (1) tuberculosis, (2) syphilis, (3) hydrocele and (4) spermatocele. 1. Tuberculosis almost always involves the epididymis, either head, body or tail. It usually is not painful but may be so and may be somewhat tender. The involved area often fixes itself to the surrounding tissues and may cause a surface area of redness, may cause edema and may form a sinus. Beading or induration of the vas may occur, as well as nodules in the seminal vesicles or the prostate. Tubercle bacilli may be found in the seminal fluid, rarely in the urine itself. 2. Two forms of syphilis are seen, one a small fibrous testis, practically never mistaken for tumor and the other a large gumma, which is frequently mistaken for a tumor. A positive serum reaction is evidence of syphilis and a blood test should be a necessary step in all cases of scrotal masses suggestive of tumor. Tumor of the testis may occur in persons having syphilis and with positive serums. If a supposed gumma does not rapidly resolve under active antisyphilitic treatment, it should be considered as a tumor of the testis. 3. Hydrocele occurs frequently by itself. It may be associated with tumor and the tumor may be discovered after the fluid is removed. Some hydroceles with thick opaque sacs, containing cholesterol plaques, at times make a differentiation difficult. 4. Spermatocele or cysts usually arise from the epididymis. They are round, elastic and not heavy and frequently can be transilluminated.

THE HORMONE TESTS IN DIAGNOSIS

The demonstration of a gonadotropic hormone in the urine of patients was first described by Zondek.[38] At first considered a reliable test, experience has shown that the amount of gonadatropic hormone with testicular tumors is determined by the amount and activity of syncytial secreting cells within the tumor. When properly performed and interpreted the test is dependable and valuable. The reaction is usually negative (less than 300 mouse units) in seminoma and negative in adult teratoma. It is positive in various stages in the teratocarcinomas and embryonal carcinomas and ranges from 500 to 10,000 mouse units, depending on the amount of syncytial tissue present. Its most valuable use is in presenting the diagnosis of choriocarcinoma in which secretions of 10,000 to over 150,000 mouse units have been recorded. A reaction to the test with gonadotropic hormone is of no value in determining cancer. A high positive reaction is conclusive of choriocarcinoma. At present the presence of hormone excreted in the urine with a testicular tumor (1) shows the presence of hormonal secreting cells and (2) may show the amount of secretory activity of the cells in tumors such as choriocarcinoma or the cellular bulk present in the less actively secreting teratomas. Thus the presence of a large amount of hormonal excretion with a small testicular tumor would imply an actively secreting tumor or many metastatic secreting cells elsewhere than the primary tumor. If no metastases are demonstrable it would be more probably from the primary tumor, probably a choriocarcinoma. By itself the presence of the hormone is no criterion for determining whether metastases are present. After the primary tumor is removed an abnormal hormonal secretion is evidence that secretory metastatic cells are present somewhere else. The presence of high hormonal secretion may show itself clinically by gynecomastia, either enlargement of nipples or breasts or both.

38. Zondek, B.: Maligne Hodentumoren und Hypophysenvorderlappenhormone, Klin. Wchnschr. 11:874, 1932; Gonadotropic Hormone in the Diagnosis of Chorioepithelioma, J. A. M. A. 106:601, (Feb. 20) 1937.

TREATMENT

Before any treatment is undertaken in testicular tumors it is essential to determine whether metastases are present. To demonstrate these a number of means are at hand. Supraclavicular (Virchow's) metastases are palpable and should be carefully looked for. Roentgenograms of the chest, preferably stereoscopic films, will show metastases to blood vessels and lung or mediastinal lymphatic masses. Retroperitoneal metastases usually are in the epigastric or hypochondriac area of the side involved. If large they may be palpable. Since the lymphatics of the testes run in the same fascial plane as the ureter and cross it and since the lymphatics near the edge of the psoas muscle or in the preaortic area may be and often are involved, some of these planes and tissues may be outlined roentgenographically. Changes of shape of the edge of the psoas and deflections of the ureter or renal pelvis can be shown by an intravenous urogram, and when present with testicular tumor are usually due to metastases. At times with intravenous pyelograms a deflection of the kidney may be noticed. Occasionally the ureter may become involved by tumor and show by obstruction to the ureter at that level on the pyelogram. It is regrettable, but a considerable number of cases show evidence of metastases when first seen.

If no metastases are demonstrable then surgical treatment may be considered. Simple orchidectomy offers a cure in the rare noncancerous adult teratomas. It may also cure an early cancer that as yet has no extension to the lymphatics. It may also offer a positive pathologic type of diagnosis in cases of suspected metastases to determine the amount and course of roentgen ray therapy. It is the prevailing surgical procedure of large numbers of surgeons, who remove the testicle complete with its coverings through a high inguinal incision with division and ligation of the cord as the primary steps before the handling of the tumor. After removal of the testis and with healing and recovery, roentgen therapy is or is not given, depending on the tumor, the therapeutist and the patient.

There is a number of surgeons who believe that a removal of the lymph nodes of the lumbar and preaortic area with the fascial planes of the spermatic vessels should be done at the same time as the removal of the testis. This is recommended only if no demonstrable masses are present. In numbers of these so removed, microscopic metastases have been demonstrated. The extension of the operation from a simple orchidectomy to this "radical orchidectomy" in the hands of its proponents has not led to any increase in the operative mortality and has given a greater percentage of freedom from recurrence than any other method. It is not at all suitable in the presence of demonstrable metastases, especially if they are without the area possible of removal. Study has shown that in autopsy in terminal cases there are widespread metastases but that the routes of these in early cases is often through lymph channels not difficult to extirpate sufficiently. The operation is especially of value in the early teratocarcinomas or mixed tumors because of their well recognized resistance to roentgen therapy. Although seminomas are radiosensitive, surgical removal of early seminomas by radical removal is preferable because their slower growth, their remaining stablized in nodes for some time and lack of infiltration make removal of these nodes not difficult.

ROENTGEN THERAPY

As in the case of the pathologic and other classifications of testicular tumors, a classification of the methods of radiotherapy for these testicular tumors is difficult. For a while there seemed to be as many radiologic technics for treating testicular tumors as there were radiologists. However, since the work of Dean and others, changes have occurred based on experience and end results. There is still uncertainty as to the relative value of preoperative radiation. Dean [39] has presented statistics that appear to demonstrate that in his group of all types of testicular tumors, the survival rate for the patients who had received preoperative irradiation was higher than that for patients who had received irradiation only after orchidectomy. Subsequent to the course of preoperative therapy, orchidectomy is performed about five to six weeks later. Preoperative irradiation has been opposed by some authors, including Smith, Dresser and Mintz,[40] Hinman and Powell [41] and MacKenzie and Ratner.[42]

Postoperative radiation after the primary orchidectomy has been widely used. Since the advent of the technic of protracted fractional doses of roentgen rays, this method or some modification of it has been most often employed. An increasing number of clinics use higher voltage in the treatment of testicular tumors as well as in other cancers. Others are of the opinion that the radiation is best carried out at potentials of the so-called moderate voltages (Nash and Leddy [36]).

It is the consensus that roentgen therapy is of primary importance in the management of seminoma of the testis and has profoundly altered its prognosis. The results apparently are far different in the teratocarcinomas or mixed tumors which have shown a more variable resistance to the therapy. Recently more massive doses over longer periods have been suggested and used for these teratoids. Complicating damage to the stomach, intestines, liver and kidneys have occurred, but with the known fatal termination of these tumors when they have metastases, the risk of visceral damage is justified.

PROGNOSIS

For all practical purposes all neoplasms of the testicle are cancerous, with the prognosis for teratoid carcinomas poorer than that for seminomas. Simple castration by itself is not the therapeutic step of choice; in about 5 per cent of cases there is freedom from recurrence for more than five years. The radical operation in selected cases with experienced workers has given the highest percentage of relief. However, a large number of patients when seen have metastases and in these surgical treatment and radiation have resulted in a freedom from recurrence in a hopeful number of cases. Such cases may show tumor awakening and extension as late as ten years after therapy.

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39. Dean, A. L., Jr.: New Methods of Irradiating Bladder Tumors, J. Urol. 41:609, 1939.
40. Smith, G. G.; Dresser, R., and Mintz, E. R.: Radiation Treatment of Tumors of the Testicle, J. Urol. 34:462, 1935.
41. Hinman, F., and Powell, T. O.: The Management of Tumor of the Testicle, J. A. M. A. 110:116, (Jan. 15) 1938.
42. MacKenzie, D. W., and Ratner, M.: Metastases from Tumors of the Testis, J. Urol. 41:592, 1939.

Clinical Notes, Suggestions and New Instruments

AUREOMYCIN IN OCULAR INFECTIONS

A Preliminary Report

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and
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In recent months, a mold belonging to the Streptomyces group has been isolated by workers[1] at the Lederle Laboratories, American Cyanamid Company. The antibiotic derived from this mold has been named "aureomycin," and numerous tests against gram-positive as well as against gram-negative organisms have strongly suggested that it might have an unusual degree of potency and range of activity. On the basis of information regarding the fundamental investigations[2] which the Lederle Laboratories provided us, it seemed desirable to test aureomycin in patients suffering with external diseases of the eye.

This new antibiotic has been used in 100 cases of ocular disease. For the most part, aureomycin was administered locally as a 0.5 per cent solution of a borate salt having a *Pu* of 7.5 to 7.8 when dissolved in isotonic sodium chloride solution. The 0.5 per cent solution of the antibiotic was only mildly irritating to the noninflamed eye and was entirely nonirritating to the inflamed conjunctiva. The chemical properties of the drug will be described elsewhere, and this report is an attempt to evaluate its use as a local antibiotic. In a later study, the antibiotic activity of aureomycin will be compared with such other antibiotics as penicillin and streptomycin and with the locally administered sulfonamide drugs.

The borated solution is stable in the powder form but unstable in solution, although it retains most of its activity when kept at + 4 C. In solution and at room temperature, the activity of the drug disappears in approximately twenty-four hours. Because of this rapid inactivation, it was felt that frequent use of the drug over a short period of time was the best method of application therefore, the majority of patients were treated for twenty-four to forty-eight hours. In a few instances a fresh supply of the antibiotic was furnished for use over a longer period. A few of the patients were given aureomycin hydrochloride intramuscularly in varying amounts, and the antibiotic in the doses used was entirely nontoxic to the patients.

The conjunctival sac of nearly all the patients was cultured for the presence of bacteria, and in some instances tissue culture and mice were inoculated in an effort to demonstrate the causative agent. In some of the patients it was not possible to determine the causative agent since several are unknown, such as vernal conjunctivitis and the Mooren's ulcer of the cornea.

STAPHYLOCOCCIC INFECTIONS

Of the patients treated, 56 had conjunctivitis produced by staphylococci either alone or combined with other organisms. Most of these patients had associated blepharitis and many had superficial punctate keratitis. The majority of patients with staphylococcic infection with associated blepharitis and keratitis were entirely healed within the first twelve to twenty-four hours. Many of the patients wtih staphylococcic conjunctivitis claimed to have had a remarkable effect within a matter of a few hours. Several of the patients were physicians who had had recurrent conjunctivitis for many years and who had become therapeutic nihilists. They were emphatically enthusiastic about the antibiotic and thought that the cure was even more rapid than with penicillin. No other form of treatment was given to patients with staphylococcic conjunctivitis associated with blepharitis. No attempt was made to remove the crusts from the lid border except for culture purposes, and following the use of the drug for approximately twenty-four hours these crusts were stained yellowish. When the antibiotic therapy was discontinued, some of the patients had recurrences within thirty-six to seventy-two hours; however, if it could be replenished and used for two days, the number of recurrences decreased.

INFLUENZAL CONJUNCTIVITIS

Following the use of aureomycin in 4 cases of influenzal conjunctivitis, there were no recurrences. Recoveries occurred in less than twenty-four hours in all instances and were more rapid than with the usual form of therapy, since all the patients reported that there was no purulent discharge from the conjunctiva following the few applications of the antibiotic.

PNEUMOCOCCIC CONJUNCTIVITIS

Five patients with pneumococcic conjunctivitis were treated. After using aureomycin every hour for sixteen hours, they were entirely free of symptoms; there were no recurrences. As far as the clinical use of aureomycin is concerned, it was effective in pneumococcic conjunctivitis.

INCLUSION CONJUNCTIVITIS

Two patients with inclusion conjunctivitis have been treated with excellent results. The discharge, which had been profuse, was entirely gone within twelve hours, and the conjunctiva returned to normal within a week when "aureomycin" was used for forty-eight hours.

EPIDEMIC KERATOCONJUNCTIVITIS

Aureomycin was given to 13 patients in whom a positive diagnosis of epidemic keratoconjunctivitis could be made. Two patients were treated three days after the onset of symptoms, and both began to show immediate response. In 1 patient, S. G., the epidemic keratoconjunctivitis virus was isolated from a specimen obtained before treatment was started. She was treated with hourly drops and with 40 mg. intramuscularly, and the symptoms were entirely gone within a week. A few corneal opacities subsequently developed in each eye, but the clinical disease was shortened. Another patient, F. M., was given "aureomycin borate" locally, beginning on the third day of the disease. He was given a fresh supply every other day and used the antibiotic for two weeks. The acute phase of the disease was shortened, and after three weeks an occasional corneal opacity developed.

The majority of patients with epidemic keratoconjunctivitis were treated after the fifth day of the disease and received no beneficial effect. In none of these was the conjunctiva changed by continual application of the antibiotic. Three patients were treated after the disease had run its course, because of the presence of corneal opacities. Two of these patients were seen after the corneal opacities had developed and one when the conjunctivitis had begun to disappear, but blurring of vision due to edema of the cornea was severe. There is no effect from the antibiotic when treatment is started after the disease is established.

Diseases Treated with Aureomycin and Number of Cases

Disease	No. of Cases
Staphylococcic conjunctivitis (aureus and albus)	56
Epidemic keratoconjunctivitis	13
Follicular conjunctivitis (unknown causation)	9
Pneumococcic conjunctivitis	5
Influenzal conjunctivitis	4
Vernal conjunctivitis	4
Dendritic keratitis (herpes simplex)	4
Inclusion conjunctivitis	2
Mooren's ulcer	2
Parinaud's conjunctivitis	1
Total	100

This paper was submitted for publication May 4, 1948.
From the Departments of Ophthalmology and Bacteriology, College of Physicians and Surgeons, Columbia University, New York.

1. Duggar, B. M., and Hesseltine, C. W.: Personal communication to the authors.
2. Wong, S. C., and Cox, H.: Personal communication to the authors.

DENDRITIC KERATITIS

Four patients with dendritic ulcers of the cornea have been treated. One patient gave a history of previous ulcers which had been dendritic in character, requiring cauterization. She was advised to return as soon as symptoms were noted. A foreign body sensation developed about six hours before her next examination. There was a typical dendritic figure in the lower part of the cornea with epithelial infiltration around the area of the ulcer. It was decided to use aureomycin locally for twenty-four hours, 1 drop at hourly intervals. The cornea was healed (except for one small area) in twenty-four hours, and forty-eight hours later the cornea was entirely clear. A child was admitted to the hospital for cautery of a dendritic ulcer and given aureomycin hourly overnight; by the time the patient was to go to the operating room for curettage of the ulcer, no ulcer could be observed. It is possible that both of these patients recovered spontaneously. The third patient was improved; the fourth showed little or no improvement following the prolonged use of aureomycin.

VERNAL CONJUNCTIVITIS

One patient with typical vernal conjunctivitis presented a large central corneal ulcer, the cause of which could not be determined. The ulcer healed promptly, and the patient observed that there was a decrease in the amount of itching and discharge as long as aureomycin therapy was continued. When treatment with the antibiotic was discontinued, there was a recurrence of itching and secretion. Because of this experience, 3 other patients with vernal conjunctivitis were treated with aureomycin borate. Two of these patients stated that they were relieved of symptoms as long as treatment with the antibiotic was continued, but the only objective difference was the lack of membrane on the conjunctiva. One patient with vernal conjunctivitis of some duration, who had received considerable roentgen therapy and in whom keratitis sicca subsequently developed, was unable to tolerate aureomycin locally.

ACUTE FOLLICULAR CONJUNCTIVITIS (CAUSE UNKNOWN)

There were 9 patients with acute follicular conjunctivitis treated with aureomycin. Studies of these patients failed to demonstrate a causative agent. All of the patients responded well to therapy, although some may have recovered spontaneously, and there were no recurrences. The period of morbidity was never beyond forty-eight hours.

PARINAUD'S CONJUNCTIVITIS

One patient with typical Parinaud's conjunctivitis was treated without beneficial effect. The normal progress of the disease was not shortened by the topical application of "aureomycin borate."

MOOREN'S ULCER

Two patients with marginal undermining advancing ulcers were treated. One had a typical Mooren's ulcer in one eye and was treated with penicillin, sulfonamide drugs, streptomycin and delimiting keratotomies, but the ulcer continued to extend, finally perforating, and the cornea became scarred. When the other eye became involved, the same treatment was instituted, but the ulcer was not controlled. Within forty-eight hours after local use of aureomycin there was no further extension of the ulcer, and the eye became clear; however, in spite of the continued use of aureomycin it was felt that the ulcer may have been extending and the treatment was discontinued.

The second patient had an atypical Mooren's ulcer that was a complete annular ulcer extending through the anterior two thirds of the cornea with an overhanging edge. The central area of the cornea was edematous and gray, and the ulcer in the second eye covered approximately two fifths of the lower part of the cornea. He was given penicillin locally and generally, and the cornea seemed to melt and the ulcer to extend. Scrapings were obtained from the margin of the ulcer and inoculated into tissue culture and subsequently into mice. He was then given intramuscular and local aureomycin therapy every hour. There was no further progression of the ulcer, and the one eye became white within a week. The eye in which there was decided edema of the central plug of the cornea became moderately opaque, although the ulcer was controlled. The upper half of the cornea cleared, with the central area clearing as the upper half of the ulcer healed. The only opaque area remaining in the cornea was the lower half; this healed by pressure dressing. The vision improved from light perception to 20/50 in this eye and in the other eye from hand movements to 20/30. The tissue culture was contaminated with a gram-negative rod and staphylococci, and it was impossible to determine the exact cause of the ulcer.

COMMENT

Aureomycin appears to be an effective antibiotic agent against most of the gram-positive staphylococci. It seems to be at least as effective as penicillin when used locally. One disadvantage of its use in staphylococcic infections, particularly those associated with blepharitis, is that the solution is not present on the lid borders in very high concentration; if the crusts on the lid are stained yellow it is more effective. The use of the antibiotic in ointment form is being investigated. Another disadvantage of the compound when used in staphylococcic infections is recurrence, since the antibiotic is used for a short time. Recurrences, however, were no more frequent than with other antibiotics. Aureomycin is effective in all staphylococcic infections, provided that it can be used over a period of several days.

In influenzal conjunctivitis aureomycin produced excellent results, and it is much more effective than penicillin or the sulfonamide drugs. Within twenty-four hours the conjunctiva had returned to normal, and within a matter of hours the secretion was entirely absent.

Its effect when used locally in inclusion conjunctivitis is good; it seems to be more effective than the local use of sulfonamide drugs and as effective as the combination of oral and local treatment with sulfonamide drugs.

No patients with trachoma were treated in this series, but from previous experience it is anticipated that the antibiotic should be effective in this disease.

Use of the material in epidemic keratoconjunctivitis looks somewhat promising, although considerably more investigation will be necessary in order to determine its therapeutic effect. From the few patients treated, it would appear that the antibiotic may be effective during the first few days of the disease, but it will not prevent the development of a moderate number of corneal opacities. After the disease is established there is doubt that the antibiotic is effective. This is probably due to the fact that the virus is fixed in the tissue and aureomycin is not available to the cell in high enough concentration.

Its effectiveness in dendritic keratitis is inconclusive, although in this series 3 patients with clinical dendritic ulcers responded satisfactorily.

It is probable that the effect of aureomycin on vernal conjunctivitis is due entirely to the control of the secondary infection and not directly to the control of the cause of the conjunctivitis.

The solution was well tolerated by all of the patients; only occasionally did it produce irritation. Intramuscular injection of aureomycin hydrochloride is only slightly irritating and in the amounts used produces no changes in the blood picture or in the urine. No allergies and no toxic effects have been encountered.

CONCLUSIONS

1. Aureomycin borate in 0.5 to 1 per cent solution is nonirritating to the inflamed conjunctiva and only slightly irritating to the noninflamed conjunctiva.

2. Aureomycin borate is effective in 0.5 per cent concentration against staphylococci, pneumococci, influenza and inclusion conjunctivitis.

3. The antibiotic appears to be effective in cases of Mooren's ulcer and atypical Mooren's ulcer of unknown cause.

4. Aureomycin has some effect in epidemic keratoconjunctivitis, provided that treatment is started before the fourth day of the disease.

5. Aureomycin may be of value in dendritic keratitis.

6. Aureomycin is a valuable addition to our armamentarium of antibiotics.

Council on Physical Medicine

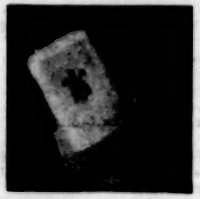
The Council on Physical Medicine has authorized publication of the following reports.

HOWARD A. CARTER, *Secretary.*

MEARS AUROPHONE HEARING AID MODEL 200 ACCEPTABLE

Manufacturer: Mears Radio Hearing Device Corp., 1 West Thirty-Fourth Street, New York 1.

Two forms of this hearing aid were submitted by the firm and subjected to adequate tests: (*a*) a model with crystal receiver, distinguished by a red grill cloth and (*b*) one with magnetic receiver, marked by a yellow grill cloth. The former model weighed 160 Gm. (5⅓ ounces); the latter 170 Gm. (5⅔ ounces). The dimensions in each case were 110 by 18 by 68 mm. (4⅜ by ¾ by 2⅝ inches). Both are plastic-cased self-contained hearing aids, and in each a hinged bottom allows the entire front side to swing down to expose the batteries and instrument proper. The microphone is structurally isolated from the chassis by rubber band suspension. The receiver is connected to the instrument by a plastic-covered nonreversible cord with plugs at the ends.



Aurophone Model 200

For the A battery, each device requires two 1.5 volt dry cells of the zinc-carbon type in series; for the B battery, a 22.5 volt source.

1. *Crystal Receiver.*—The power consumption of this instrument was measured in an independent laboratory and was found to be 21 milliamperes at 2.9 volts for the A battery. For the B battery at 22 volts, the consumption was 0.29 milliampere when quiet and 0.16 milliampere in the presence of sound. Acoustical gain was also measured. The data here tabulated represent the decibel difference between the sound pressure at the face of the microphone of the instrument and the pressure produced by the receiver in a 2 cc. coupler. The pressure at the face of the microphone was held at approximately 60 decibels above zero for these measurements (60 decibels above 0.0002 dyne per square centimeter) and the volume control was set at "full." Readings were made at seven different frequencies and three settings of the tone control:

	Frequencies						
Tone	200	500	1,000	1,200	2,200	3,000	4,000
1	Noise	42	57	50	38	39	30
2	Noise	28	49	43	33	33	25
3	Noise	28	40	29	25	23	14

The following are approximate values of maximum sound pressure levels (at three frequencies) in a 2 cc. coupler with the volume control set for full gain and the tone control set at position 1:

Frequency	Input Level	Maximum Output Level
600	90	126
1,000	90	140
2,600	90	132

Intelligibility tests were made with a person of normal hearing seated inside a booth giving about a 30 decibel sound reduction. The speaking person was outside the booth using normal speaking voice. Score made with the Harvard no. 9 lists under these critical conditions was 95 per cent.

2. *Magnetic Receiver.*—The power consumption of this instrument was similarly measured and found to be 29 milliamperes at 2.9 volts for the A battery. For the B battery at 22 volts, the consumption was 0.49 milliampere when quiet and 0.42 milliampere in the presence of sound. Measurements of acoustical gain were made under the conditions described, with the following results:

Tone	200	500	1,000	1,200	2,200	3,000	4,000
1	39	50	52	55	41	53	40
2	Noise	30	42	46	36	49	36
3	Noise	30	42	46	36	49	32

The following are approximate values of maximum sound pressure levels, at three frequencies, in a 2 cc. coupler with the volume control set for full gain and the tone control set at position 1:

Frequency	Input Level	Maximum Output Level
600	90	132
1,000	90	132
1,300	85	132

Intelligibility tests were made with a person of normal hearing seated inside a booth giving about a 30 decibel sound reduction. The speaking person was outside the booth using normal speaking voice. Score made with the Harvard no. 9 lists under these critical conditions was 80 per cent.

The Council on Physical Medicine voted to include the Mears Aurophone Hearing Aid, Model 200, with crystal and magnetic receivers, in its list of accepted devices.

MAICO D-9 AUDIOMETER ACCEPTABLE

Manufacturer: The Maico Company, Inc., North Third Street, Minneapolis 1.

The Maico Audiometer, Model D-9, is a discrete frequency instrument designed to present pure tone stimuli at 64, 128, 256, 512, 1,024, 2,048, 2,896, 4,096, 5,792, 8,192 and 11,584 cycles per second for the clinical testing of hearing. In general arrangement it resembles the previously accepted Model D-5, which it is intended to supersede. The instrument is encased in a wood cabinet and has an inclined panel. Controls are clearly marked and arranged as in the D-5.

The audiometer weighs 11.3 Kg. (25 pounds) and measures 45.4 by 25 by 19.4 cm. (17⅞ by 9⅞ by 7⅝ inches). The carrying case weighs 6.8 Kg. (15 pounds) and measures 63 by 29 by 22 cm. (25 by 11½ by 8¾ inches).

Maico D-9 Audiometer

The D-9 model is supplied with both air and bone conduction receivers, a signal switch for responses by the patient, a masking circuit that feeds a magnetic head phone, a speech circuit for communicating with severely hard of hearing patients and a headband for the various receivers.

The instrument was tested in two types of situation, one a clinic where routine audiometric tests were given to hard of hearing patients, and the other a field program for testing adults. In addition, measurements were made of air conduction thresholds yielded by normal ears, bone conduction thresholds for the same, aerial radiation from the bone receiver, efficiency of masking tone, properties of the attenuation system, wave form of signal and residual noise. Results of these tests indicated that the instrument was satisfactory in both types of situation.

The Council on Physical Medicine voted to include the Maico Audiometer, Model D-9, in its list of accepted devices.

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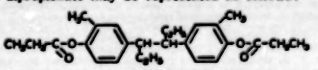
Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

PROMETHESTROL DIPROPIONATE. — Meprane Dipropionate-Reed & Carnrick.—Dimethylhexestrol dipropionate. — 3,4 - Bis - (*m*-methyl-*p*-propionoxyphenyl) hexane. — $C_{28}H_{36}O_4$.—M. W. 410.53.—The structural formula of prometh estrol dipropionate may be represented as follows:



Actions and Uses.—Promethestrol Dipropionate is similar in its actions to diethylstilbestrol and other synthetic estrogens. It is used for the same conditions for which estrogenic substances are employed and the contraindications are those of the natural estrogens.

Dosage.—In the menopause, treatment may be started with 1 mg. given three times daily, gradually reducing the dosage to 1 mg. daily. For suppression of lactation, 3 to 5 mg. daily.

Tests and Standards.—

Promethestrol dipropionate occurs as a white, odorless crystalline powder, melting between 113 and 116 C. It is freely soluble in benzene, ether and ethyl acetate; slightly soluble in alcohol; and practically insoluble in water, dilute acids and dilute alkalis. A solution of promethestrol dipropionate in 90 per cent alcohol is neutral to litmus.

Dissolve about 10 mg. of promethestrol dipropionate in 1 cc. of sulfuric acid; an orange-red solution is obtained. Dilute (*caution!*) with 10 cc. of water: a pink, turbid solution is formed, which becomes white after standing for several minutes (*distinction from benzestrol, diethylstilbestrol, ethyl estradiol, hexestrol and mestilbol.*)

Add 1 drop of ferric chloride T.S. to 2 cc. of a saturated solution of promethestrol dipropionate in diluted alcohol. The color is no different than that obtained by adding ferric chloride T.S. to the solvent (*distinction from benzestrol, diethylstilbestrol, hexestrol and mestilbol, which give a slight greenish-yellow color when the reagent is added*).

Dry about 1 Gm. of promethestrol dipropionate, accurately weighed, in a vacuum desiccator over phosphorus pentoxide at room temperature for 24 hours: the loss in weight does not exceed 0.5 per cent.

Char about 0.5 Gm. of promethestrol dipropionate accurately weighed, over a low flame. Cool, then add 1 cc. of sulfuric acid and continue ignition until no carbon remains: no more than 0.05 per cent of residue results.

Place about 0.25 Gm. of promethestrol dipropionate, accurately weighed, in a 125 cc. Erlenmeyer flask containing 10 cc. of 0.5 *N* alcoholic sodium hydroxide. Reflux gently for 2 hours, cool and titrate the excess base with 0.1 *N* sulfuric acid, using phenolphthalein T.S. as indicator. The saponification equivalent (obtained by dividing the mass of promethestrol dipropionate used in milligrams by the number of cc. of 1 *N* sodium hydroxide consumed in the saponification) is not less than 203 nor more than 210.

Add about 75 cc. of water and 2 cc. of sulfuric acid to the samples used in determining the saponification number. Distil and collect about 50 cc. of the distillate. Titrate a 10 cc. portion (A) of the distillate with 0.01 *N* sodium hydroxide. Redistil the remaining 40 cc. of distillate, collecting three 10 cc. fractions (B, C, D). Titrate each fraction with 0.01 *N* sodium hydroxide. The Duclaux numbers 10B/A, 10C/A and 10D/A should be between 10 and 12.

Accurately weigh about 0.25 Gm. of promethestrol dipropionate, previously dried to constant weight over phosphorus pentoxide, and reflux this sample for 1 hour in 10 cc. of 15 per cent methanolic potassium hydroxide. Cool, add 100 cc. of water and quantitatively transfer the solution to a separatory funnel. Acidify with 10 per cent hydrochloric acid and extract with four 50 cc. portions of ether. Wash the combined ether extracts with three 100 cc. portions of 5 per cent sodium bicarbonate and with two 100 cc. portions of water. Filter the ether solution into a tared beaker, wash the funnel and filter paper once with ether and then evaporate slowly on a water bath to constant weight. The weight of 3,4-bis(*m*-methyl-*p*-hydroxyphenyl)hexane obtained, when multiplied by 1.376, is equal to not less than 98.5 nor more than 101.5 per cent of the weight of promethestrol dipropionate taken for analysis. The 3,3'-dimethylhexestrol thus obtained melts between 150 and 158 C.

The 3,3'-dimethylhexestrol obtained in the previous assay is dissolved in 5 cc. of 5 per cent sodium hydroxide and 1 cc. of benzoyl chloride is added slowly with constant shaking. Continue shaking for 10 minutes after the addition of the benzoyl chloride and then add diluted ammonia solution until a distinct ammoniacal odor is present. Shake for an additional 10 minutes, remove the solid by filtration, wash several times with water and then with ethanol, and dry. The 3,3'-dimethylhexestrol dibenzoate obtained melts between 200 and 208 C.

PROMETHESTROL DIPROPIONATE TABLETS: Accurately weigh a sufficient number of promethestrol dipropionate tablets to contain 50 mg. of the drug and grind them to a powder. Transfer an accurately weighed quantity of this powder, equivalent to about 20 mg. of the drug, to a 50 cc. glass-stoppered graduated cylinder. Extract the solid by shaking with four 20 cc. portions of ether. Allow the suspended material to settle after each extraction. Decant the ether and filter into a tared beaker. Wash the filter paper with a 20 cc. portion of ether, collecting it in the same beaker as the extracts. Evaporate the combined filtrates and dry the residue to constant weight in a vacuum desiccator over phosphorus pentoxide. The quantity of 3,4-bis-(*m*-methyl-*p*-propionoxyphenyl)hexane is not less than 90 nor more than 110 per cent of the labeled amount.

The extracted material responds to the identification tests listed in the monograph on promethestrol dipropionate.

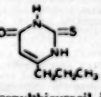
Small amounts of promethestrol dipropionate may be determined colorimetrically. A quantity of powdered tablet material sufficient to contain 1 mg. of the drug is weighed accurately and transfered to a 125 cc. Erlenmeyer flask containing 10 cc. of alcohol and three drops of sulfuric acid. Reflux the suspended material for 2 hours and quantitatively transfer the contents to a 100 cc. volumetric flask. Wash the Erlenmeyer flask with three 10 cc. portions of diluted alcohol and add the washings to the volumetric flask. Add 2 cc. of diluted hydrochloric acid and 4 cc. of molybdo-phosphotungstate T.S. and 20 cc. of water. Shake the mixture thoroughly and allow to stand for 10 minutes. Add 10 cc. of 25 per cent sodium carbonate (anhydrous) and dilute to 100 cc. with water. Shake and then allow the reaction mixture to stand for about 1 hour. Filter the solution and compare at 580 mμ with a standard and blank run simultaneously with the unknown.

REED & CARNRICK, JERSEY CITY, N. J.

Tablets Meprane Dipropionate: 1 mg.

U. S. patent applied for.

PROPYLTHIOURACIL. — 6-propyl-2-thiouracil. — $C_7H_{10}N_2OS$.—M. W. 170.226. The structural formula of propylthiouracil may be represented as follows:



Actions and Uses.—Propylthiouracil interferes with the formation of thyroxin by the thyroid gland. It is useful in the treatment of hyperthyroidism, thyrotoxicosis and thyroiditis. It is of no value and should not be used in other derangements of thyroid activity or in conditions not associated with hyperthyroidism.

Since propylthiouracil does not inactivate or interfere with the action of thyroxin already formed and stored in the gland, the effects of propylthiouracil medication do not appear until this store of thyroxin has been utilized. It may take several days to several weeks for the signs of decreased thyroid activity to become manifest, particularly if the patient has received previous iodine therapy.

Not all patients experience a permanent remission following propylthiouracil therapy, and the duration of treatment necessary to secure permanent relief from hyperthyroidism has not been determined. On the basis of the available information, it can be recommended only that propylthiouracil be used for preoperative treatment or for those patients for whom operation is contraindicated. The wisdom of depending on propylthiouracil as a substitute for operative procedure can be determined only by following the results of investigations carried on for longer periods.

Propylthiouracil is capable of producing adverse reactions in some patients. The incidence and severity of these reactions are unpredictable, but they occur with less frequency than do those following medication with the parent compound, thiouracil. The severest complication of propylthiouracil therapy is granulocytopenia. Less severe reactions may include leukopenia, drug fever and dermatitis. The drug should be discontinued and appropriate therapy commenced immediately on the detection of signs of any of these complications.

Since the mild and the juvenile types of hyperthyroidism can frequently be controlled adequately by iodine therapy alone, propylthiouracil should not be used for these patients unless the safer form of therapy proves ineffective.

Dosage.—For severe cases of hyperthyroidism, initial doses of 50 mg. of propylthiouracil every eight hours appear to be effective in routine treatment, and 50 mg. twice daily in milder cases. Iodine should be administered for two or three weeks immediately before thyroidectomy.

The effective dosage of propylthiouracil should be continued until all signs and symptoms of the disease have been brought under control. Adequate maintenance dosage may best be established by determinations of the basal metabolic rate. *Patients should be instructed to cease medication and report to their physician immediately if any adverse symptoms such as sore throat, fever, coryza or malaise are experienced.*

Tests and Standards.—

Propylthiouracil occurs as a bitter, white, powdery, crystalline substance of starchlike appearance to the eye and to the touch. It melts sharply in the range of 218 to 220 C. It is sparingly soluble in alcohol,

slightly soluble in chloroform and ether, very slightly soluble in water and practically insoluble in benzene.

Add 1 cc. of strong ammonia solution to 25 mg. of propylthiouracil: complete solution occurs *(25 mg. of thiouracil will not completely dissolve in 1 cc. of strong ammonia solution)*.

Slowly add bromine water to about 25 mg. of propylthiouracil in a test tube until complete solution is effected. Discharge the color with heat. Cool and add 10 cc. of barium hydroxide T. S.: a white precipitate forms *(distinction from thiouracil, which yields a white precipitate that turns purple within a minute)*.

Dry 0.5 Gm. of propylthiouracil, accurately weighed, to constant weight at 100 C.: the loss in weight does not exceed 0.5 per cent.

Char about 0.5 Gm. of propylthiouracil, accurately weighed; cool, add a few drops of sulfuric acid to the cooled mass and ignite: the amount of residue is not more than 0.1 per cent.

Add 4 cc. of water and 1 cc. of silver nitrate T. S. to 0.5 Gm. of propylthiouracil in a test tube. Add 5 cc. of nitric acid and allow the solution to stand until the reaction is complete. Expel the oxides of nitrogen by heating; dilute with 10 cc. of water, and cool to room temperature: the turbidity does not exceed that of 0.1 cc. of fiftieth-normal hydrochloric acid used as a control *(chlorides)*.

Heat 25 cc. of water containing 0.5 Gm. of propylthiouracil for ten minutes on a steam bath. Cool, filter and wash the filter paper; adjust the volume of the filtrate to 25 cc. with the washings. Add 1 cc. of barium chloride T. S. and 1 cc. of diluted hydrochloric acid: the turbidity does not exceed that of 0.1 cc. of fiftieth-normal sulfuric acid used as a control *(sulfates)*.

Dissolve 1 Gm. of the propylthiouracil in sufficient sodium hydroxide T. S. to give complete solution, and dilute to 20 cc. with water. Add 5 drops of sodium sulfide T. S.: no more turbidity develops than corresponds to 20 parts per million of lead *(U. S. P. XIII)*.

Weigh, accurately, about 0.5 Gm. of propylthiouracil and transfer to a 400 cc. beaker containing 100 cc. of neutralized alcohol. Add 5 drops of phenolphthalein T. S. Slowly titrate with tenth-normal sodium hydroxide, stirring constantly until complete solution is effected. Continue the titration to the first visible pink color. Each cubic centimeter of tenth-normal sodium hydroxide solution is equivalent to 0.01702 Gm. of propylthiouracil: the propylthiouracil content is not less than 95 nor more than 105 per cent.

PROPYLTHIOURACIL TABLETS: Weigh, accurately, 20 propylthiouracil tablets and grind them to a fine powder. Transfer about 400 mg., accurately weighed, to a 400 cc. beaker containing 100 cc. of neutralized ethyl alcohol. Add 5 drops of phenolphthalein T.S. Slowly titrate with tenth-normal sodium hydroxide, stirring constantly. Continue the titration to the first visible pink color. Each cubic centimeter of tenth-normal sodium hydroxide solution is equivalent to 0.01702 Gm. of propylthiouracil: the propylthiouracil content is not less than 93 nor more than 105 per cent of the claimed amount.

ABBOTT LABORATORIES, NORTH CHICAGO, ILL.

Propylthiouracil Tablets: 25 mg. and 50 mg.

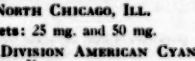
LEDERLE LABORATORIES DIVISION AMERICAN CYANAMIDE CO., PEARL RIVER, NEW YORK

Tablets Propylthiouracil: 50 mg.

THE UPJOHN COMPANY, KALAMAZOO, MICH.

Tablets Propylthiouracil: 50 mg.

METHIONINE.—"Meonine"-Wyeth.—DL-Methionine.—γ-Methylthiol-α-aminobutyric acid.—$C_5H_{11}NO_2S$.—M. W. 149.21.—The structural formula for DL-Methionine may be represented as follows:



Actions and Uses.—Methionine is a sulfur containing amino acid which is considered to be an indispensable dietary component. It is available in synthetically prepared racemic form that may be administered in sufficient quantity to provide amounts equivalent to the biologically active levo form.

In animal experiments, certain deficient diets, especially those low in protein and high in fat, will cause liver damage in almost all animals, and, in addition, renal damage in some. That these pathological changes can be prevented by the addition to the diet of methionine alone is of great theoretical interest; similar protection can be obtained by casein, and doubtless by other common foodstuffs, as less rigorously restricted diets do not produce hepatic lesions.

Severe liver damage is regularly caused in protein depleted dogs by chloroform anesthesia and this is altogether prevented by methionine. Lean beef and other high protein diets are equally effective. A similar protective effect has been demonstrated against other hepatotoxic agents such as oxophenarsine in animal experiments.

The striking results of these animal experiments have led to the use of methionine in the treatment of liver disease in man, especially in hepatic cirrhosis, acute hepatitis and toxic hepatitis due to carbon tetrachloride and T.N.T. poisoning. In all these studies, methionine was used as a supplement to other standard methods of treatment such as high protein diet and vitamins. The improvement which sometimes follows cannot be attributed to the methionine alone.

There is at present no valid evidence that pure methionine is superior as a therapeutic agent to a high protein diet containing foodstuffs, such as casein and eggwhite, which contain methionine in large amounts. But because of its great theoretical interest and in the hope that some special utility may be found, methionine has been accepted for experimental purposes only.

Of low toxicity, the use of methionine is not likely to be attended by any untoward effects.

Dosage.—As a supplement to a high protein diet, 3 to 6 Gm. daily is usually administered in tablet form. In severe cases 10 to 20 Gm. has been used. When oral administration is not feasible, crystalline methionine may be given in amounts of 5 to 10 Gm. daily by slow intravenous drip as a 3 per cent solution in Dextrose Injection, U. S. P., or Water for Injection, U. S. P., that has been further sterilized by autoclaving.

Tests and Standards.—

DL-Methionine occurs as white, crystalline platelets or a powder, having a faint odor. It is soluble in water, dilute acids and dilute alkalis; very slightly soluble in alcohol; and practically insoluble in ether. A 1 per cent aqueous solution of DL-methionine exhibits a pH in the range 5.6-6.1, and is optically inactive.

Dissolve 4.5 Gm. of DL-methionine in 150 cc. of water. The solution is clear and colorless. To 25 cc. of this solution add 1 cc. of diluted hydrochloric acid and 2 cc. of barium chloride T. S. The turbidity is less than that shown by 0.4 cc. of 0.02 *N* sulfuric acid diluted to 25 cc., and treated in a similar manner *(sulfate)*. To another 25 cc. portion add 1 cc. of nitric acid and 1 cc. of silver nitrate T. S. The turbidity is not more than that obtained when 0.2 cc. of 0.02 *N* hydrochloric acid is diluted to 25 cc., and treated in the same manner *(chloride)*. Add 1 cc. of 1 *N* sodium hydroxide and 1 drop of Nessler's reagent T. S. to 25 cc. of the DL-methionine solution: the color developed is less than that produced by 25 cc. of a solution containing 0.0125 mg. of ammonium chloride *(ammonium salts)*. Add 1 cc. of 4 *N* hydrochloric acid to 25 cc. of the solution and then add 10 cc. of hydrogen sulfide T. S. The color produced is less than that obtained when 1.5 cc. of lead solution *(U. S. P. XIII)* is diluted to 25 cc., acidified and treated with hydrogen sulfide T. S. *(heavy metals)*. To the solution containing DL-methionine, used in the test for heavy metals, add 2 cc. of ammonia T. S.: the green color obtained is no darker than that produced by treating the blank from the heavy metals test with 1 cc. of ferric chloride solution containing about 0.05 mg. of iron (made by diluting 1 cc. of ferric chloride volumetric solution, *U. S. P. XIII*, to 200 cc.), mixing, and adding 2 cc. of ammonia T. S.

Add about 25 mg. of dry DL-methionine to about 1 cc. of saturated solution of anhydrous copper sulfate in sulfuric acid: the appearance of a yellow color indicates methionine.

Dissolve about 5 mg. of DL-methionine in 5 cc. of water and then add in succession, shaking after each addition, 1 cc. of 5 *N* sodium hydroxide, 1 cc. of 1 per cent glycine, and 0.3 cc. of 10 per cent sodium nitroprusside (freshly prepared). Keep at 35-40 C. for 10 minutes, and then cool in an ice-bath for 2 minutes. Add 2 cc. of 20 per cent hydrochloric acid and shake the mixture: the appearance of a reddish-purple color indicates methionine.

Dry about 1.5 Gm. of DL-methionine, accurately weighed, at 100 C. for 4 hours: the loss in weight does not exceed 0.5 per cent.

Char about 1 Gm. of DL-methionine, accurately weighed, over a low flame. Cool, add 1 cc. of sulfuric acid and continue ignition until no carbon remains: the residue does not exceed 0.05 per cent.

Transfer about 0.1 Gm. of dry DL-methionine, accurately weighed, to a semi-micro Kjeldahl flask and digest with 5 cc. of sulfuric acid, 2 Gm. of potassium sulfate, 0.2 Gm. of copper sulfate and 1 cc. of 30 per cent hydrogen peroxide. Dilute the clear solution to 10 cc., make alkaline with 40 per cent sodium hydroxide, and distil the ammonia into 50 cc. of 0.02 *N* sulfuric acid. Titrate the excess acid with 0.02 *N* sodium hydroxide, using methyl red T. S. as an indicator: the nitrogen content is not less than 9.2 nor more than 9.5 per cent.

Weigh, accurately, about 0.3 Gm. of DL-methionine, transfer quantitatively to a 100 cc. volumetric flask and fill to the mark with distilled water. Transfer a 5 cc. portion of the solution to an Erlenmeyer flask and add 2 cc. of borate buffer (7 volumes of 1 M $KaHPO_4$ and 3 volumes of 1 M $KHaPO_4$) and 2 cc. of iodine solution, approximately 0.1 *N*. Permit the mixture to stand for about 15 minutes and then remove the excess iodine with 0.1 M sodium thiosulfate solution, using starch-potassium iodide T. S. as an indicator. Add 2.5 cc. of 2 *N* hydrochloric acid and titrate the iodine liberated with 0.025 *N* sodium thiosulfate. Perform a blank determination on 5 cc. of the DL-methionine solution as follows: add 1 cc. of 6 *N* hydrochloric acid and enough 0.1 M potassium iodate solution to give a persistent yellow color. Allow the solution to stand for about 15 minutes and then add 1 cc. of 5 *N* potassium iodide solution. Add about one-half the sodium hydroxide needed for neutralization (3 cc. of 1 *N*) followed by a mixture of the remainder of the sodium hydroxide and 3 cc. of the phosphate buffer. Add 2 cc. of 5 *N* potassium iodide solution and allow to stand for 5 minutes. Remove the excess iodine with 0.1 M sodium thiosulfate solution, add 2 cc. of 2 *N* hydrochloric acid and titrate the iodine liberated. Subtract the amount of thiosulfate used in the blank from that used in the determination: 1 cc. of 0.025 *N* sodium thiosulfate is equivalent to 0.001865 Gm. of methionine. The percentage of methionine should be not less than 98.3 nor more than 101 per cent.

TABLETS: The pulverized tablets respond to the identification tests and assay described in the monograph on DL-Methionine. Each tablet should contain not less than 95 nor more than 105 per cent of the claimed amount of DL-methionine.

WYETH INCORPORATED, PHILADELPHIA

Crystalline Meonine *(Powder)*: 50 Gm. bottles.

Tablets Meonine: 0.5 Gm.

U. S. trademark 406,890.

SODIUM ASCORBATE INJECTION U. S. P. (See New and Nonofficial Remedies 1947, p. 520).

The following dosage form has been accepted:

THE CENTRAL PHARMACAL CO., SEYMOUR, IND.

Solution Sodium Ascorbate: 100 mg. per cc., 10 cc. vials.

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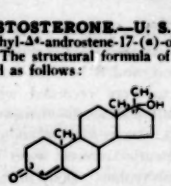
METHYLTESTOSTERONE.—U. S. P.—17-Methyltestosterone.—17-methyl-Δ^4-androstene-17-(α)-ol-3-one.—$C_{20}H_{30}O_2$.—M. W. 302.44. The structural formula of methyltestosterone may be represented as follows:



For description and standards see the U. S. Pharmacopeia under Methyltestosterone and Methyltestosterone Tablets.

Actions and Uses.—Methyltestosterone may be given orally in the treatment of gonadal failure in the male. Its actions and uses are qualitatively the same as those for testosterone proprionate.

Dosage.—The dosage and duration of methyltestosterone therapy vary considerably, depending on the condition, its severity, previous androgenic administration and individual variation. It is usually preferable to begin therapy with a low dose, about 5 mg. daily, increasing to 10 mg. or 15 mg. if higher doses appear indicated.

RARE CHEMICALS, INC., HARRISON, N. J.

Tablets Methyltestosterone: 10 mg. and 20 mg.

ALUMINUM HYDROXIDE GEL (See New and Nonofficial Remedies 1947, p. 315).
The following dosage has been accepted:

WM. R. RORER, INC., PHILADELPHIA

Tablets Dried Aluminum Hydroxide Gel (Flavored): 0.3 Gm.

CHORIONIC GONADOTROPIN (See New and Nonofficial Remedies 1947, p. 374).
The following dosage form has been accepted:

ENDO PRODUCTS, INC., RICHMOND HILL, N. Y.

Estromone *(Powder):* 5,000 I. U. and 10,000 I. U., 10 cc. vials. Powdered preparations of chorionic gonadotropin, which when diluted with 9 cc. of the accompanying isotonic solution of sodium chloride and preserved with phenol 0.4 per cent, provides solutions having a potency of 500 or 1,000 international units per cc. respectively.

U. S. patent 1,910,298; U. S. trademark 354,550.

DIENESTROL (See THE JOURNAL, Nov. 22, 1947, p. 773).
The following additional dosage form has been accepted:

WHITE LABORATORIES, INC., NEWARK, N. J.

Aqueous Suspension Dienestrol: 5 mg. per cc., 10 cc. vials. Preserved with chlorobutanol 0.5 per cent.

U. S. patent applied for.

ESTROGENIC SUBSTANCES (WATER INSOLUBLE) (See New and Nonofficial Remedies 1947, p. 343).
The following dosage forms have been accepted:

BIORGANIC LABORATORIES, INC., BROOKLYN

Estrogenic Substances: Bulk.

ENDO PRODUCTS, INC., RICHMOND HILL, N. Y.

Aqueous Suspension Estromone: 20,000 I. U. per cc., 10 cc. vials.

THE NATIONAL DRUG CO., PHILADELPHIA

Solution Estronate in Oil: 5,000 I. U. per cc. in corn oil, 10 cc. Injectosols; 10,000 I. U. per cc. in corn oil, 1 cc. ampuls, 10 cc. and 25 cc. Injectosols; and 20,000 I. U. per cc. in corn oil, 10 cc. and 25 cc. Injectosols. Preserved with chlorobutanol 0.5%.

PROCAINE HYDROCHLORIDE (See New and Nonofficial Remedies, 1947, p. 57).
The following dosage form has been accepted:

LINCOLN LABORATORIES, INC., DECATUR, ILL.

Solution Procaine Hydrochloride 2%: 100 cc. vial. Each cubic centimeter contains procaine hydrochloride 2 per cent in distilled water. Preserved with chlorobutanol 0.5 per cent.

MEPERIDINE HYDROCHLORIDE (See New and Nonofficial Remedies 1947, p. 28).
The following additional dosage form has been accepted:

WINTHROP-STEARNS, INC., NEW YORK

Tablets Demerol Hydrochloride: 100 mg.

PERTUSSIS VACCINE (See New and Nonofficial Remedies 1947, p. 457).
The following dosage form has been accepted:

CUTTER LABORATORIES, BERKELEY, CALIF.

Pertussis Vaccine: 20,000 million *H. pertussis* per cc., 5 cc., 20 cc. and 50 cc. vials; and 40,000 million *H. pertussis* per cc., 2.5 cc., 10 cc. and 25 cc. vials. Preserved with sodium ethyl mercuri thiosalicylate 1:10,000 and phenol 0.25 per cent.

PENICILLIN (See New and Nonofficial Remedies 1947, p. 144).
The following dosage forms have been accepted:

E. R. SQUIBB & SONS, NEW YORK

Crystalline Procaine Penicillin G in Oil: 300,000 units in peanut oil, 1 cc. and 10 cc. vials suspended with 2% aluminum monostearate; 1 cc. double-cell cartridges with Aspirating Test Solution preserved with chlorobutanol 0.5 per cent in packages of five cartridges; 1 cartridge with disposable syringe and needle and 1 cartridge with sterile hypodermic needle alone for use with metal B-D cartridge syringe assembly.

ABBOTT LABORATORIES, NORTH CHICAGO, ILL.

Crystalline Penicillin G Potassium: 100,000, 200,000, 500,000 and 1,000,000 unit vials.

BIO-RAMO DRUG COMPANY, BALTIMORE

Penicillin Calcium in Oil and Wax: 300,000 units per cc., 10 cc. vials.

PREMO PHARMACEUTICAL LABORATORIES, NEW YORK

Crystalline Procaine Penicillin G in Oil: 300,000 units per cc., in sesame oil, 10 cc. vials.

HUMAN SERUM IMMUNE GLOBULIN.—The gamma globulin fraction of normal adult human plasma. The finished product contains 16.5% of gamma globulin and complies with the minimum requirements of the National Institute of Health and as prepared by an acceptable method.

Actions and Uses.—For modification or complete protection against measles.

Dosage.—The volume of the dose per pound of body weight is 0.02-0.025 cc. for modification and at least 0.1 cc. for prevention when the product contains 150 mg. of gamma globulin per cc.

CUTTER LABORATORIES, BERKELEY, CALIF.

Immune Serum Globulin (Human): 2 cc. vials. Preserved with sodium ethyl mercuri thiosalicylate 1:10,000.

Licensed by Research Corporation. U. S. patent No. 2,390,074.

POISON IVY-SUMACH EXTRACT.—A solution of the combined resin extracted from the fresh leaves of Rhus toxicodendron rodicon and Rhus toxicodendron vernix.

Actions and Uses.—Poison Ivy-Sumach Extract is used for prevention of the symptoms of the dermatitis produced through contact with Rhus toxicodendron rodicon and Rhus toxicodendron vernix.

Dosage.—Three injections of 0.1 cc., 0.2 cc. and 0.4 cc. on successive days.

BARRY LABORATORIES, INC., ALLERGY PRODUCTS DIVISION, DETROIT

Poison Ivy-Sumac Extract: Packages of four vials each containing 0.7 cc. of concentrated extract and three vials each containing 0.9 cc. diluent; also in 15 cc. vials of concentrated extract. The diluent contains 0.5% procaine hydrochloride, and is preserved with 0.4% chlorobutanol in physiologic solution of sodium chloride.

Preparation.—

The oily substance which is extracted with suitable solvents from the fresh leaves of Rhus toxicodendron rodicon and Rhus toxicodendron vernix is purified and decolorized. The resultant oily resin is dissolved in alcohol and standardized to represent a 1:500 dilution.

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SATURDAY, OCTOBER 9, 1948

CHLOROMYCETIN

From a soil sample collected in a mulched field near Caracas, Venezuela, Burkholder [1] of Yale University isolated a new strain of Streptomyces. Agar streak cultures of this organism were found to inhibit adjacent inoculums of a wide variety of gram-positive and gram-negative micro-organisms, including: Bacillus subtilis, S. aureus, Brucella abortus, Escherichia coli, Klebsiella pneumoniae, Salmonella schottmuelleri and Shigella paradysenteriae. When the Burkholder Streptomyces was grown in shaken flasks of liquid mediums, filtrates proved to possess antibacterial activity in broth dilutions against the same micro-organisms. From these filtrates a crystalline product was isolated, which was named "chloromycetin."

This crystalline material inhibits the growth of a wide range of gram-positive and gram-negative bacteria when tested in dilutions as high as 0.35 microgram per cubic centimeter. This is a higher effective dilution than that of the earlier antibiotics. Of particular interest was his observation that chloromycetin when injected into chick embryos shows chemotherapeutic activity against several rickettsial and virus diseases. Similar therapeutic results were noted in infected mice. Moreover, in contrast with streptomycin, chloromycetin is rapidly absorbed from the gastrointestinal tract of laboratory animals, and is apparently nontoxic even when given intravenously in massive doses.

More detailed studies of the therapeutic effects of this new antibiotic were undertaken by Smadel and Jackson [2] of the Army Medical Center, Washington, D. C. Initial tests were performed with groups of twenty-four 7 day embryonated eggs, infected by the yolk sac route with Rickettsia orientalis, Rickettsia prowazeki, Rickettsia mooseri or Dermacentroxenus rickettsi. Eggs were examined daily and the time of death noted. All untreated control eggs died of the infection. It was found that as little as 0.125 mg. chloromycetin given at the time of infection would definitely prolong life. Doses as large as 1 mg. per egg would reduce the mortality by at least 65 per cent. Sixteen of the 24 treated eggs survived to the fifteenth day after infection, and 8 hatched normally. Similar therapeutic effects were recorded with embryonated eggs infected with psittacosis virus, variola virus or influenza A virus.

Similar therapeutic effects were noted in mice infected with scrub typhus. Daily intraperitoneal injections of as little as 0.1 mg. per mouse, started one day after infection, reduced the mortality by 62.5 per cent, while 1.5 mg. doses similarly given reduced the mortality to zero. With a 2.5 mg. intraperitoneal dose, the treatment could be delayed for five to eight days and still be equally effective. If delayed till the tenth day this intraperitoneal dose would save but 60 per cent of the infected mice. By doubling the dosage chloromycetin was equally effective if given orally. Chloromycetin was equally effective with mice infected with Japanese encephalitis.

So far as noninfected control mice and embryonated eggs which received the maximum doses of chloromycetin remain unaffected, the new antibiotic is apparently without appreciable toxicity. On account of this apparently low toxicity, the ready absorption of chloromycetin from the alimentary tract and its beneficial effects when given relatively late in experimental disease, Smadel and his associates suggested that chloromycetin might be of value in human medicine.

As a preliminary to a proposed study of its therapeutic value, Smadel [3] and his associates administered single or repeated oral doses to a group of physician volunteers. After a single dose of 2 Gm. appreciable amounts of the drug were demonstrable within thirty minutes in both blood and urine. The titers decreased to zero by the end of eight hours. From this rapid elimination of the drug frequent oral administration is indicated in order to maintain the antibiotic at an appreciable level in the blood stream. With a 1 Gm. initial dose followed by 0.2 Gm. doses every four hours, the antibiotic can be maintained at an effective level in the blood. Approximately 10 per cent of the total amount thus given was recovered in active form from the urine. Toxic effects were not observed by the volunteer physicians during or after such administration.

After this preliminary work on normal volunteers a group of 5 patients with typhus were treated with the same oral doses.[4] The diagnosis was confirmed by positive Weil-Felix and specific rickettsial agglutination reactions. Treatment was begun between the fifth and the eighth day of the disease. At this time three of the patients exhibited a high grade fever, high pulse rate and a plus 2 to plus 3 rash. One patient was in delirium. Each patient was given an initial oral dose of 1 to 2 Gm. chloromycetin, followed by a 0.2 Gm. oral dose every four hours. In all cases there was a

1. Ehrlich, J.; Bartz, Q. R.; Smith, R. M.; Joslyn, D. A., and Burkholder, P. R.: Science **106**: 417, 1947.
2. Smadel, J. E., and Jackson, E. B.: Science **106**: 418, 1947.
3. Ley, H. L.; Smadel, J. E., and Crocker, J. T.: Proc. Soc. Exper. Biol. & Med. **68**: 9 (May) 1948.
4. Smadel, J. E.; Leon, A. P.; Ley, H. L., and Varela, G.: Proc. Soc. Exper. Biol. & Med. **68**: 12, 1948.

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rapid fall in pulse rate and body temperature. The delirium disappeared within three days. The rash disappeared within three to five days. Toxic reactions were not noted.

Comparison was made with an equal number of patients with typhus not treated with the new antibiotic. On the basis of these limited comparisons Smadel and his associates concluded that the administration of chloromycetin to patients with typhus is a safe procedure and that the therapeutic effects are sufficiently encouraging to warrant further tests of the drug with rickettsial and virus diseases.

More extensive tests of this drug were made by the Malaya Institute of Medical Research, during the recent outbreak of scrub typhus at Kuala Lumpur.[5] Twenty-five hospitalized patients were treated with chloromycetin, while 12 untreated hospitalized patients served as controls. Treatment was begun on an average 6.2 days after the onset of the infection. All treated patients became afebrile within an average of thirty hours after the initial dose. The untreated patients remained febrile for an average of eighteen days. Rickettsemia disappeared within twenty-four hours after the initial dose, and the rash within forty-eight hours. All treated patients were discharged from the hospital on an average of thirteen days after beginning the treatment. The untreated controls remained on an average for 30.7 days after onset. No complications or deaths were noted with the 25 treated patients. Among the 12 untreated controls, in 2 complications developed (parotitis, pneumonia), and 1 died.

According to the daily press even more spectacular therapeutic effects were afterward obtained during an outbreak of epidemic typhus in Bolivia. Details are not yet reported.

THE AERO MEDICAL ASSOCIATION

The Aero Medical Association met at Royal York Hotel and R. C. A. F. Institute of Aviation Medicine, Toronto, Canada, June 16-18, 1948. Among the papers presented that of E. E. Poos, Detroit, pointed out that certain ocular symptoms, such as blurring, burning, light flashes, photophobia, vertigo, amaurosis fugax, disturbances of muscles, accommodation, convergence, migraine, glaucoma and central angiospastic retinopathy are frequently of psychosomatic origin, reflecting ocular symptoms of certain conversion syndromes. Among these may be mentioned guilt, conflict, fear, pain, indecisiveness, feelings of inferiority and fatigue reactions.

Ryan and his associates at the R. C. A. F. Institute of Aviation Medicine, Toronto, reported physiologic findings in normal men subjected to negative G.[1] The outstanding symptoms under negative G and the limiting symptom by which the subject decides that his safe G tolerance is reached is pressure in the head region. Visual symptoms commonly include blurring, graying and more specifically reddening of vision. The pulse rate decreases under negative G and the greater the negative G the more pronounced the bradycardia. The pulse rate quickly increases again as the negative G decreases. On repeated negative tilts on six successive days men acquired a subjective tolerance for negative G, and the average pulse rate on the last negative tilts was significantly lower than on the first, suggesting a physiologic adaptation as the basis of this increased tolerance. A similar acquired tolerance was experienced on repeated exposures to the higher negative G values studied. Despite the absence of subjective cardiac symptoms, electrocardiograms from precordial leads showed increasing deviations from the normal with increasing negative G. These consisted of arrhythmias, prolonged P-R intervals, auriculoventricular heart block and bizarre QRS complexes, but most strikingly of periods of cardiac asystole (up to nine seconds' duration). Under the experimental conditions used it was demonstrated that healthy young men can with safety withstand 3 G negative for five seconds.

J. C. Douglas, of the University of Western Ontario, London, Canada, reported studies on pulmonary function with the use of the Milliken oximeter. He found that in normal subjects an alveolar oxygen tension of approximately 210 mm. of mercury produces complete saturation. This corresponds roughly to 35 per cent oxygen in the inspired air. The time to reach saturation is about forty seconds. In subjects with pulmonary dysfunction, significant differences in respect to both these measurements have been found. Henry and his associates at the Aero Medical Laboratory, Wright-Patterson Air Force Base, Dayton, Ohio, studied the effect of breathing high pressures on the circulation. The main effects were (1) the loss of plasma filtrate into the tissues and (2) pooling of blood with diminished venous return. Loss of fluid was estimated by means of hematocrit and hemoglobin determinations, and venous pooling by two methods: (1) a modification of the Evan's blue blood volume technic and (2) a water displacement plethysmograph. An immediate (first four minutes) effect of pressure breathing is pooling of approximately 7 per cent of total blood volume. A further loss of 10 per cent results from plasma filtration during a thirty minute period, making a total of approximately 15 to 20 per cent of total blood volume lost from effective circulation.

Haymaker and his co-workers reported on pathologic changes believed to have been due to hypoxia in 75 fatal cases of high altitude hypoxia. The pathologic changes were divided into three categories: (1) vascular phenomena including congestion, edema and hemorrhage; (2) vacuolar changes, with and without inclusion bodies, in parenchymal cells of various internal organs,

5. Smadel, J. E.; Woodward, T. E.; Ley, H. L., Jr.; Philips, C. B.; Traub, R.; Lewthwaite, R., and Savoor, S. R.: Science **108**: 160, 1948.

1. The terms "positive and negative G" are arbitrary ones used to designate the direction in which the G force is acting in relationship to the longitudinal axis of a human being. Positive "G" refers to "G" acting on the body in a direction from head to foot, while negative "G" refers to "G" acting in a direction from foot to head. The common sources of "G" are gravity, from which the term "G" is derived, and centrifugal force such as is encountered in flying.

and (3) reactive and degenerative changes in the central nervous system.

F. G. Hall, Duke University, Durham, N. C., presented an interesting study of various factors which affect the time interval between loss of oxygen and loss of useful consciousness in persons at simulated high altitudes. Factors investigated were barometric pressure, pulmonary ventilation, breathing pattern and composition of the blood. Striking differences occurred between individuals in useful consciousness times which appeared consistent from day to day but do not correlate with any factors so far studied. Smith and Law of University of Toronto made an interesting suggestion for meeting the emergency of sudden decompression of a pressurized passenger transport when flying at high altitude. The proposed method of meeting the emergency is to flood the cabin with oxygen gas, obtained by spraying liquid oxygen against a suitable evaporating surface. The weight of liquid oxygen required has been calculated, and is no greater than that of an emergency oxygen gas system. A safe breathing atmosphere can be produced within two minutes at 40,000 feet. If the aircraft promptly starts to descend, safety can be maintained in spite of a large outward leak.

W. R. Stovall, Civil Aeronautical Administration, Washington, D. C., stressed the responsibility of flight surgeons in the selection, welfare, health and safety of all flight personnel. The rapid growth of aeronautics calls for more flight surgeons; yet the number of surgeons is diminishing. Approximately 500 flight surgeons in the armed services, together with reservists in civilian practice, constitute the national pool. Several suggestions were made with the view of maintaining or increasing this pool.

Current Comment

"ANTIVIVISECTIONISTS HAVE NO VALID ARGUMENTS"

As predicted[1] when the antivivisectionists were exposed by the *Saturday Evening Post*,[2] the latter magazine was deluged with mail, some of which was commendatory, and some condemnatory. One antivivisectionist went so far as to threaten to use his rifle on experimenters. The *Post* publishes two columns of letters *pro* and *con*; one demands: "Answer yes or no. Are you or are you not going to print the other side of the vivisection question?" The following answer of the editors of the *Post* to this demand is significant: "We made an exhaustive study of the pros and cons of vivisection before we published 'They're Trifling with Your Life.' Not one valid argument in support of the antivivisectionist viewpoint was found. This being the case, we feel no obligation to publish anything more than the comments in these columns."[3] This ought to settle the antivivisectionist argument, but it will not. The antivivisectionists are not capable of being convinced, and continued vigilance by physicians and other scientists will be necessary. The antivivisectionists need constant watching even though they have not thus far achieved important legislative results.

1. Antivivisectionists Exposed, Editorial, J. A. M. A. 138:132 (Sept. 11) 1948.
2. Moon, V. H., and Wittels, D. G.: They're Trifling with Your Life, Sat. Eve. Post 221:16 (July 24) 1948.
3. Letters to the Editor: Sat. Eve. Post 221:4 (Aug. 28) 1948.

ORIGIN OF PILONIDAL SINUS

A theory that most pilonidal sinuses are acquired infective and foreign body granulomatous reactions to buried hair rather than developmental malformations was recently proposed by Patey and Scarff.[1] They point out serious defects in the evidence for the developmental theory. A few sacrococcygeal dermoid cysts which are apparently developmental in origin unquestionably occur. They are located between the rectum and the coccyx; they are first noted in early life, and they are rarely infected. Pilonidal sinuses, on the other hand, are found chiefly in the intergluteal cleft; they first appear in young life, and they are almost invariably infected. About half of them contain hair; many have no epithelial lining; few show hair follicles in their walls, and fewer still show sebaceous glands. In the absence of these structures, there is no evidence for origin from dermoid. Postoperative recurrences may contain hair, yet have no epithelial cells. They may be so large that they could not have been left behind by an incomplete operation; they must have enlarged, probably under the influence of the hairs. The number of recurrences appears to be reduced by postoperative roentgen treatment. The suggestion is made that the role of such therapy may be to destroy the hair follicles. Finally, Patey and Scarff describe 3 examples of pilonidal sinus in the hands of barbers. These sinuses, except for their shorter length, resembled those in the postanal region. They contained hair which had apparently penetrated through the skin and set up a foreign body reaction, and there was no suspicion of preexisting dermoid. The authors suggest that a similar process might produce postanal pilonidal sinuses. The deeper penetration of the hair in both locations is attributed to the sucking action of negative pressures produced by passive motion of the adjacent tissues. This new theory is more attractive for explaining the pathogenesis of the pilonidal sinuses of the hand than of those in the postanal region. In the former, the hairs found in the sinus are short—a few millimeters. In the latter, they may be several centimeters long, indicating that they have grown. Therefore, they were attached and not free to migrate. The high incidence of a dimple in the postanal region of children at the location where the pilonidal sinus later develops indicates the presence of at least one type of malformation in these cases; so, presumably, there could be another. Finally, it is not clear why hair should penetrate and set up pilonidal sinuses only in the hand and the postanal region.

1. Patey, D. H., and Scarff, R. W.: Pathology of Postanal Pilonidal Sinus: Its Bearing on Treatment, Lancet 2:484 (Oct. 5) 1946; Pilonidal Sinus in a Barber's Hand with Observations on Postanal Pilonidal Sinus, ibid. 2:13 (July 3) 1948.

ORGANIZATION SECTION

World Medical Association

Second General Assembly, Geneva, Sept. 8-11, 1948

The World Medical Association held its Second General Assembly in Geneva, September 8 to 11. This important association includes practically all of the national medical organizations, thus constituting a world organization of physicians. The association aims to elevate medical ethics and the standard of medical education throughout the world. It hopes to defend the status of the physician against encroachment by the state, and to perfect medical organization and to make it more effective.

The 1948 General Assembly was to meet in Prague under the presidency of Professor Jaroslav Stuchlik. Recent political events in Czechoslovakia resulted in the dissolution of the Czechoslovakian Medical Association and in resignation of Dr. Stuchlik.

The General Assembly was opened on September 8 by M. Picot, President of the National Swiss Council. Dr. Routley of Canada, chairman of the Council of the World Medical Association, proposed that Professor Eugene Marquis of France be president of the association for the year 1948-1949.

Unified Medical Diploma

Several months ago Dr. L. H. Bauer (United States), general secretary, sent an inquiry to various national medical associations requesting their views concerning the establishment of a medical diploma which would be recognized in all of the countries of the world. This proposition was originated by Dr. Guy Dain of Great Britain. The majority of the countries felt that the idea was excellent but not practical. The assembly voted to abandon Dr. Dain's proposition.

The War Crimes of the German Doctors

At the previous assembly in Paris the World Medical Association solemnly condemned the crimes and the inhuman acts committed by the German physicians, and invited them to make a declaration which would recognize that a number of their colleagues "have violated the ethical traditions of medicine, defiled the professional medical honor and prostituted medical science by placing it at the service of war and political hatred." There is not now in Germany any national medical organization that could speak for the physicians of Germany.

The Hippocratic Oath

The inhuman acts perpetrated by certain physicians testified to the regrettable lowering of medical ethics. The World Medical Association believes that reestablishment of the original Hippocratic Oath or of its modern version to be read by the doctor on the receipt of his diploma would aid in impressing on him the fundamental principles of medical ethics and would tend to elevate the general level of professional practice. Dr. Cibrie (France) presented a convincing argument in favor of adoption of a modern version of the Oath. On motion of Dr. Pridham (England), seconded by the Danish delegate, the General Assembly adopted a motion that the name of the city of Geneva be included in the official text of the modified Hippocratic Oath. Following is the text of the Oath in French as formulated in Geneva with a proposed English text:

SERMENT D'HIPPOCRATE, FORMULE DE GENÈVE

Au moment d'être admis au nombre des membres de la profession médicale, je prends l'engagement solennel de consacrer ma vie au service de l'humanité.

Je garderai à mes maîtres le respect et la reconnaissance qui leur sont dus.

J'exercerai mon art avec conscience et dignité.

Je considérerai la santé de mon patient comme mon premier souci.

Je respecterai le secret de celui qui se sera confié à moi.

Je maintiendrai, dans toute la mesure de mes moyens, l'honneur et les nobles traditions de la profession médicale.

Mes collègues seront mes frères.

Je ne permettrai pas que des considérations de religion, de nation, de race, de parti ou de classe sociale viennent s'interposer entre mon devoir et mon patient.

Je garderai le respect absolu de la vie humaine, dès la conception.

Même sous la menace, je n'admettrai pas de faire usage de mes connaissances médicales contre les lois de l'humanité.

Je fais ces promesses solennellement, librement, sur l'honneur.

THE HIPPOCRATIC OATH FORMULATED AT GENEVA

Now being admitted to the profession of medicine I solemnly pledge to consecrate my life to the service of humanity. I will give respect and gratitude to my deserving teachers. I will practice medicine with conscience and dignity. The health and life of my patient will be my first consideration. I will hold in confidence all that my patient confides in me. I will maintain the honor and the noble traditions of the medical profession. My colleagues will be as my brothers. I will not permit considerations of race, religion, nationality, party politics or social standing to intervene between my duty and my patient. I will maintain the utmost respect for human life from the time of its conception. Even under threat I will not use my knowledge contrary to the laws of humanity. These promises I make freely and upon my honor.

The Bulletin of the World Medical Association

Dr. Charles Hill, secretary of the British Medical Association, presented a well documented report on the subject of creating a bulletin of the World Medical Association. The bulletin will appear four times annually, will contain a résumé of the papers presented at the Council and at the General Assembly, and will report on subjects of medicosocial nature. Dr. Routley (Canada), President of the Council, announced that Dr. Morris Fishbein (Chicago), the Editor of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, is to be the chief editor of the bulletin.

Relations with Other International Organizations

The World Medical Association intends to maintain most cordial relations with the great international organizations, in particular with the World Health Organization and with UNESCO. The World Medical Association has appointed two permanent observers whose duty will be to report on the activities of these organizations. Dr. Maystre (Geneva), president of the Medical Association of Geneva, will report on the international organizations' meeting in Geneva; Dr. Cibrie (Paris), recording secretary of the World Medical Association for Europe, will report the discussions of the UNESCO. Dr. Calderone of New York, replacing Dr. Chisolm, has reported the aims of these great organizations and presented in an extensive table the activities and the aims of the World Health Organization.

Coming Meetings of the World Medical Association

The General Assembly decided to hold the 1949 meeting in London; the 1950 meeting in the United States, city not designated; and the 1951 meeting in Stockholm. In case of inability on the part of any of these nations to serve as the meeting place, Spain will be ready to receive the delegates.

Discussion of the Subject of Social Insurance

Social insurance is in process of expansion almost everywhere, and particularly in Europe. The International Association for Social Security and the International Labour Organization appear to be resolved to encourage a complete program of social insurance, embracing medical service for the entire world. The Council of the World Medical Association recommended

to the General Assembly at Geneva the initiation of an extensive inquiry, detailed and precise, to be reported on by the national medical associations with the view of arriving at correct information on the status of the subject in each country. A permanent committee on social insurance was appointed by the General Assembly. This committee will make every effort that doctors be not outdistanced in the matter of social security by the International Conference, which carries on its work on a permanent scale. It is a matter of regret that because of lack of organization doctors always find themselves faced with accomplished facts when it is too late to suggest and to bring about modifications of decisions already taken.

Several delegates presented in the course of discussion upon this subject rather general ideas for social insurance schemes in their respective countries

Recommendations

The following resolutions were adopted at the General Assembly in Geneva as fundamental in any system of social security.

a. **Freedom of choice of physician by the patient. Liberty of physician to choose patient except in cases of urgency or humanitarianism.**
b. **No intervention of third party between physician and patient.**
c. **Where medical service is to be submitted to control, this control should be exercised by physicians.**
d. **Freedom of choice of hospital by patient.**
e. **Freedom of the physician to choose the location and type of his practice.**
f. **No restriction of medication or mode of treatment by physician except in case of abuse.**
g. **Appropriate representation of medical profession in every official body dealing with medical care.**
h. **It is not in the public interest that physicians should be full time salaried servants of the government or Social Security bodies.**
i. **Remuneration of medical services ought not to depend directly on the financial condition of the insurance organization.**
j. **Any Social Security or insurance plan must be open to the participation of any licensed physician, and no physician should be compelled to participate if he does not wish to do so.**
k. **Compulsory health insurance plans should cover only those persons who are unable to make their own arrangements for medical care.**
l. **There shall be no exploitation of the physician, the physician's services or the public by any person or organization.**

World Medical Association and Scientific Research

In Canada, in the United States of America and in England are councils of medical research. The Assembly decided to request the most immediate and extensive diffusion possible of the results of these researches.

The Question of Refugee Doctors

The General Assembly listened to a communication of Dr. Coigney, Medical Advisor of the International Organization of Refugees in Geneva. Among the total of 800,000 "displaced persons" there are about 3,000 doctors between the ages of 25 and 45 years. Dr. Coigney requested the assembly to propose to various governments to pass definite laws to authorize these doctors to practice their arts after having passed examinations and after having obtained naturalization. The speaker invoked the seventh paragraph of the Hippocratic Oath adopted by the assembly. In the name of the Council, Dr. Routley emphasized the importance of the question and proposed to submit it at the next meeting of the Council.

The Council of the World Medical Association endorsed the efforts of the A.S.E.M. ("Swiss Aid to the Children of the Doctors, Victims of the War") whose office is in Geneva, and has decided to support this work so far as is possible.

The Newly Elected President

Dr. Charles Hill, honorary secretary of the British Medical Association, who has done so much for the organization of the World Medical Association, was elected by acclamation president for 1949.

Washington Letter

(From a Special Correspondent)

Oct. 7, 1948.

Displaced Professional Persons

According to the International Refugee Organization, which has headquarters in Washington, there are now 30,437 professional men and women in European D.P. camps who meet preferential requirements fixed by Congress in the Displaced Persons Act of 1948. Of this number, 1,150 are listed as physicians or surgeons. Nurses number 2,566, although complete information on the percentage of these who are registered is not available.

Volume on "America's Health"

One week after Washington offices of National Health Assembly had sent a letter to 4,200 individuals and representatives of organizations active in the public health field, 500 replies were received expressing interest in procurement of "America's Health: A Report to the Nation." This is the provisional title of the prospective volume which will present the findings of the fourteen sections participating in the National Health Assembly held here last May. According to the answers on the reply card, a 500 page volume priced at $5 is preferred over 200 pages at $4 or 600 to 700 pages at $5.50 to $6.50. The first week's 500 respondents indicated that they would be interested in purchasing a total of 2,500 copies. The volume, the fourteen sections of which are in the editing stage, is scheduled to appear between spring and fall of 1949.

Research a Challenge

Dr. Leonard A. Scheele, Surgeon General, U. S. Public Health Service, addressed the opening of the one hundred and twenty-fifth session of George Washington University School of Medicine September 20. Medical research, preventive medicine and psychiatry were singled out by Dr. Scheele as specialties in which too few students are interested. He said, "There is no greater challenge to intellectual and social pioneering in our age than research and preventive medicine. The shortages of medical investigators and medical health officers are acute, not only in the programs of the Public Health Service, but in research institutions and health departments all over the country." Dr. Scheele noted that ten graduates of George Washington University School of Medicine are now serving in the commissioned corps of Public Health Service.

Blood Plasma Distributed in Palestine

American Red Cross headquarters here has been informed that dried blood plasma donated for use in Palestine has been distributed to six principal cities. Shipped to the Middle East last July, the plasma is part of more than $500,000 worth of medical and relief supplies donated by the American Red Cross for Jewish and Arab victims of the Palestine conflict. Nazareth, Gaza, Jerusalem, Tel Aviv, Ramallah and Jericho are the cities to which the plasma was sent, under supervision of International Red Cross. Meantime, the American Red Cross is sending two ambulances to the Syrian Red Crescent to aid Arab and Jewish refugees in Syria.

New Veterans Administration Hospital at Houston

The Army Corps of Engineers has issued invitations for bids to construct a thousand bed Veterans Administration neuropsychiatric hospital to be erected at Houston, Texas. Bids are scheduled to be opened October 21 at the District Engineer's Office, Galveston.

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GOVERNMENT SERVICES

NAVY

NEW REGULAR OFFICERS

The following reserve officers have been transferred to the Medical Corps of the Regular Navy: Comdr. Thomas P. Rogers, Indianapolis; Lieut. (jg) David G. Dixon, Homestead, Pa.; Lieut. (jg) Martin D. Greaney Jr., Los Angeles; Lieut. (jg) Frank P. Hammon, Saratoga, Calif., and Lieut. (jg) Henry A. Schlang, Flushing, N. Y.

RESERVE OFFICERS ON ACTIVE DUTY

The following inactive reserve medical officers have been recalled to active duty: Lieut. Comdr. Alexander A. Bolton Jr., Lake Mohawk, Sparta, N. J.; Lieut. Comdr. William W. Manson, Sidney, N. Y.; Lieut. Gustave T. Anderson, North Platte, Neb.; Lieut. Trowbridge H. Mafit, Chicago; Lieut. (jg) Hodge M. Eagleson, Pittsburgh; Lieut. (jg) William S. Foultz, Cleveland; Lieut. (jg) Albert M. Jenkins, Norwood, Ohio, and Lieut. (jg) Francis X. MacAulay, Westminster, Mass.

The following lieutenants (jg) of the Medical Reserve Corps have received orders to report for their first active duty:

Armon A. Cairo, Shelton, Pa., to Georgetown University Hospital, Washington, for duty as intern.

Leon W. Clark, Houston, Texas, to University of Texas Hospitals, Galveston, Texas, for instruction in pediatrics.

Myron E. Erickson, Minneapolis, to Swedish Hospital, Minneapolis, for duty as intern.

Alfred K. Hawkes, New Orleans, to Tulane University of Louisiana School of Graduate Medicine, New Orleans, for instruction in otolaryngology.

Theo. N. Kirkland Jr., Montgomery, Ala., to Tulane University of Louisiana School of Graduate Medicine, New Orleans, for instruction in ophthalmology.

Charles E. Mangin, Biloxi, Miss., to Touro Infirmary, New Orleans, for instruction in pediatrics.

Harry L. Roberts Jr., Hanover, N. H., to Columbia Hospital for Women, Washington, D. C., for instruction in obstetrics and gynecology.

Paul E. Rockwell, Brooklyn, to the Administrative Command, Great Lakes, Ill., for duty in the Medical Department.

William R. Sillery, Cliffside Park, N. J., to Long Island College Hospital, Brooklyn, for instruction in obstetrics and gynecology.

Robert R. Wadlund, Wethersfield, Conn., to the Naval Hospital, St. Albans, N. Y.

POSTGRADUATE INSTRUCTION

The following officers of the Regular Navy have been nominated for courses of postgraduate instruction: Comdr. Ross P. Black, urology; Comdr. James A. Fields, otolaryngology; Comdr. Joseph A. Force, internal medicine, all at the University of Pennsylvania Graduate School of Medicine, Philadelphia; Comdr. Richard D. Nies, psychiatry, Naval Hospital, Bethesda, Md.; Comdr. Nelse O. Olson, ophthalmology, Washington University School of Medicine, St. Louis; Comdr. Joseph J. Timmes, surgery, University of Pennsylvania Graduate School of Medicine, Philadelphia; Lieut. Comdr. Wilbur S. Lummis Jr., internal medicine, Northwestern University Medical School, Passavant Hospital, Chicago; Lieuts. Don L. Andrus, surgery, University of Pennsylvania Graduate School of Medicine, Philadelphia; Edward L. Beckman, electroencephalography and neurophysiology, Naval Hospital, Bethesda, Md.; Berwyn R. Force, internal medicine, University of Pennsylvania Graduate School of Medicine, Philadelphia; Emil P. Thelen, fellowship in neurosurgery, Mayo Clinic, Rochester, Minn.; Frank H. Thomas Jr., internal medicine, University of Pennsylvania Graduate School of Medicine, Philadelphia, and Henry G. Wagner, ophthalmology, University of Pennsylvania Graduate School of Medicine, Philadelphia; Lieuts. (jg) John G. Esswein, residency in internal medicine, Naval Hospital, Philadelphia; Aubrey D. Bantt, Submarine School, New London, Conn.; Clarence H. Johnston, residency in pathology, Naval Hospital, San Diego, Calif., and Vincent E. Lowery, residency in psychiatry, Naval Hospital, Bethesda, Md. Comdrs. James G. Bulgrin, residency in radiology, Naval Medical Center, Bethesda, Md.; John L. Flannery, instruction in pediatrics, University of Pennsylvania Graduate School of Medicine, Philadelphia; William S. Francis, residency in internal medicine, Naval Hospital, Oakland, Calif., and Jesse F. Richardson, fellowship in urology, Washington University Medical School; Lieut. Comdr. Byron E. Bassham, fellowship in surgery, Lahey Clinic, Boston; Lieuts. (jg) Winton R. Boyd, residency in obstetrics and gynecology, Naval Hospital, Oakland, Calif.; Carl A. Broaddus Jr., residency in surgery, Naval Hospital, Oakland, Calif.; Harold A. Davis, MCR, residency in internal medicine, Naval Hospital, San Diego, Calif., and Andrew M. Margileth, residency in pediatrics, Naval Hospital, National Naval Medical Center, Bethesda, Md.

WOMEN IN THE NAVY MEDICAL CORPS

Among the first 288 women officers who have been selected for commissions in the Regular Navy under the provisions of the Women's Armed Services Integration Act of 1948 are 2 in the Medical Corps, 21 in the Medical Service Corps and 1 chief warrant officer in the Hospital Corps. The 2 in the Medical Corps are Lieutenant Commander Frances Lois Willoughby of Washington, D. C., a graduate of the University of Arkansas School of Medicine, Little Rock, and Lieutenant Gioconda Rita Saraniero of Brooklyn, a graduate of Women's Medical College of Pennsylvania, Philadelphia.

INTERNS AT CIVILIAN INSTITUTIONS

The Bureau of Medicine and Surgery of the Navy announces the following Naval Medical Reserve Corps officers who have received their first orders for active duty as interns in civilian institutions under the new medical training program:

Lieut. (jg) James E. Fitzgerald, Chevy Chase, Md., to Gallinger Municipal Hospital, Washington, D. C.

Lieut. (jg) James R. Martin, Pittsburgh, to Allegheny General Hospital, Pittsburgh.

Lieut. (jg) Victor A. Moore Jr., Roswell, Ga., to University Hospital, Augusta, Ga.

Lieut. (jg) Joseph H. Pritchett Jr., Decatur, Ga., to University Hospital, Augusta, Ga.

Lieut. (jg) Rob J. Rutledge, Oklahoma City, to Kansas City General Hospital, Kansas City, Mo.

Lieut. (jg) Theodore Safford Jr., Wyoming, Ohio, to Lenox Hill, N. Y.

Lieut. (jg) Emitt H. Shoemaker, Houston, Texas, to Hermann Hospital, Houston, Texas.

Lieut. (jg) Frank F. Stangl, Gallup, N. M., to Kansas City General Hospital, Kansas City, Mo.

AWARDS AND COMMENDATIONS

Commander John E. Nardini

The commanding general of the Philippine Coast Artillery Command awarded in April, 1942, the Silver Star to then Lieut. John E. Nardini of Philadelphia. The citation read as follows:

"For gallantry in action at Fort Mills, Philippine Islands, March 30, 1942. During the course of a combined enemy aerial and artillery bombardment of Fort Mills, Lieutenant Nardini, together with Pharmacist's Mate Second Class Donald E. Bansley, 2124309, U. S. Navy, without regard for his personal safety and while enemy planes were overhead, voluntarily left a place of shelter and evacuated a Marine who had been seriously wounded by shell fragments to Malinta Hospital. Dr. Nardini graduated from Temple University School of Medicine, Philadelphia, in 1938 and entered the Navy on July 18 of that year."

VETERANS ADMINISTRATION

NON-SERVICE-CONNECTED DISABILITIES

In a summary of its activities as of Aug. 31, 1948, the Veterans Administration reported a total of 105,048 patients in hospitals; of the 92,983 in Veterans Administration hospitals 61,091 were veterans with non-service-connected disabilities; of the 12,065 patients not in Veterans Administration hospitals, 7,488 were veterans with non-service-connected disabilities. In addition there were 14,342 beneficiaries in Veterans Administration homes.

Eighty-nine new hospitals were in progress at the end of August, of which the construction contracts had been awarded for 28, the designs were in progress in 50, the designs not started in 3 and the designs completed but construction contracts not awarded in 8. Through the end of the month, 63 sites have been acquired for new veterans hospitals, 20 specific sites have been approved but not acquired, 7 specific sites were in the process of selection; furthermore, 31 additions and conversions to the hospital addition and conversion program had been completed throughout the month and seventeen other additions and conversions were in progress.

At the end of August, 18,560 veterans were awaiting hospital admission; of these 18,490 had disabilities adjudicated non-service-connected; 77,277 applications for hospital or domiciliary care were received through the month, and 33,679 applications were filed for automobiles for disabled veterans.

COURSE IN REHABILITATION

Nineteen physicians from various Veterans Administration hospitals and one Army physician are enrolled in the second 3 month course of instruction in physical medicine and rehabilitation, which will continue until December 11 at the Veterans Administration Hospital, Hines, Ill. The course is under the direction of Dr. Louis B. Newman, chief of physical medicine rehabilitation service. This group visited the A. M. A. headquarters September 29 and was addressed by the directors of various departments.

NEW HOSPITAL AT ERIE, PA.

Ground breaking ceremonies were held in June marking the beginning of construction of the two hundred bed veterans general hospital at Erie, Pa., on the southwest corner of Old French Road and East 38th Street Boulevard. Among those

New Veterans Hospital at Erie, Pa.

taking part in the ceremony were Dr. Guy C. Boughton, representing the Erie County Medical Society; Capt. Henrietta Dorris, Army Nurse Corps; Dr. Joseph Galbo, representing the American Legion and Dr. Elmer Hess.

PERSONALS

Dr. J. Haywood Davis has been assigned as chief medical officer of the Veterans Administration Outpatient Clinic at Fort Worth, Texas, succeeding Dr. M. D. Badt.

Dr. Thomas J. Ready has been assigned as chief medical officer and Dr. Frank D. Thomas as chief of the outpatient medical service for the Pass-a-Grille regional area in Florida. Dr. Ready is a graduate of Georgetown University School of Medicine, Washington, D. C., and served in the Army Medical Corps during the recent war. Dr. Thomas is a graduate of Hahnemann Medical College, Philadelphia, and is a veteran of World War I.

PUBLIC HEALTH SERVICE

CONFERENCE ON GASTRIC CANCER

The National Advisory Cancer Council has called a conference on gastric cancer to be held in San Francisco December 13-14 to review research progress in this field and attempt to give direction to the development of methods of diagnosis and treatment. At one evening session of the conference, the scientists will meet with physicians of the San Francisco Bay area to discuss the clinical applications of their findings. Dr. Leonard A. Scheele, Surgeon General of the Public Health Service and chairman of the Council, said that according to official mortality records gastric cancer causes about 45 per cent of all deaths due to cancer and that the reason undoubtedly is the silent nature of the disease. "It is almost impossible," he said, "to diagnose gastric cancer in its early stages when cure might be expected."

The Public Health Service has made previous attacks on the problem of gastric cancer, having had in effect for years a program of grants-in-aid specifically planned to develop research on gastric cancer. Altogether, twenty-three grants totaling $261,424 are being devoted to research on such problems as the relation between gastric cancer and diet, the possible influence of hormones on gastric cancer and the role, if any, that pernicious anemia and ulcers play.

NEW DIRECTOR OF INDIAN HEALTH

The Surgeon General announces the appointment of Dr. Fred T. Foard as Director of Health at the Bureau of Indian Affairs of the Department of the Interior. Dr. Foard was graduated from University of Maryland Medical School and is a medical director in the United States Public Health Service.

DR. GILLIAM TO HEAD EPIDEMIOLOGY SECTION

Dr. Alexander G. Gilliam of the regular Army Medical Corps has been appointed by the Surgeon General to head the Epidemiology Section of the Cancer Control Branch, National Cancer Institute, which section was recently formed to improve information on cancer incidence and mortality. For two years Dr. Gilliam has been detailed to the University of Michigan School of Health, where he conducted studies on poliomyelitis and taught in the Department of Epidemiology. During the war he was epidemist to the United States of America Typhus Commission and was awarded the Typhus Medal for conducting typhus surveys among United States troops in Egypt, Tripoli, China, Burma and India.

CANCER RESEARCH GRANTS

The Federal Security Administrator announced September 26 National Cancer Institute grants of more than $1,300,000 to finance cancer control and research work in institutions in twenty-six states, the District of Columbia, Puerto Rico, Canada and France. These grants were first approved by the National Advisory Cancer Council and by the Surgeon General of the Public Health Service at a meeting of the council a few days previously. Twelve grants totaling $186,114 were made for such special projects as the development of laboratory diagnostic tests for cancer, surveys of occupational cancer and training in cytologic test technics. More than one hundred medical and dental schools have qualified for financial aid since the beginning of the program of the Public Health Service less than a year ago.

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Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as rebate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

CONNECTICUT

Yale University Retirements.—Retirement of three faculty members of Yale University School of Medicine, New Haven, has been announced: Dr. Arthur H. Morse, former chairman of the department of obstetrics and gynecology; Dr. George M. Smith, research associate in anatomy with the rank of professor, and Miss Alice M. Hunt, assistant professor of anesthesia. Dr. Morse, who has been departmental chairman and obstetrician and gynecologist in chief of the New Haven Unit of the Grace-New Haven Community Hospital since 1921, became assistant professor of obstetrics and gynecology at Yale in 1915 and received a promotion to clinical professor in 1920 and to professor in 1921. Dr. Smith has held the post of research associate with the rank of professor at Yale since 1936. He has been medical director of the Anna Fuller Fund, which provides research grants for investigating problems of cancer, since 1933. He is also a member of the board of scientific advisers of the Jane Coffin Childs Memorial Fund for Medical Research and is executive director of the National Advisory Cancer Council. Miss Hunt was instructor in anesthesia at Yale from 1922 to 1930 and since that time has been an assistant professor of anesthesia and anesthetist for the New Haven Unit of the Grace-New Haven Community Hospital.

FLORIDA

Cancer Seminar.—The Cancer Seminar of the Southeastern States will be held November 8-10, at the Tampa Terrace Hotel, Tampa, under the direction of the Tumor Clinic, Tampa Municipal Hospital, and sponsored by the American Cancer Society, Florida Division, and the Florida State Board of Health. The seminar will consist of morning and afternoon sessions, presenting in panel discussion carcinoma of the breast, the lung, the uterus, the ovary and the stomach. Each subject will be discussed by a surgeon or internist, a pathologist and a roentgenologist. At the end of each panel discussion thirty minutes will be allowed for questions from the audience. This seminar is conducted for the doctors of the Southeastern states and is primarily intended for the benefit of physicians in general practice; however, specialists in any field of medicine are urged to attend. Requests for hotel accommodations should be sent to Mr. A. K. Dickinson, % Tampa Chamber of Commerce, Tampa, Fla.

GEORGIA

Narcotic Violation.—The Federal Bureau of Narcotics reports that Dr. Joseph Haskell Hudson, Gough, pleaded guilty at Savannah to violation of the federal narcotic law and on May 11 was placed on probation for a period of three years.

Courses in Diagnosis of Rabies.—The Public Health Service Communicable Disease Center at Atlanta will offer a course in the laboratory diagnosis of rabies December 6-10, open to all grades of employed laboratory personnel. There is no tuition or laboratory fee, but traveling and living expenses must be paid by the individual or his employer. Applications should be made to Ernest S. Tierkel, 605 Volunteer Building, Atlanta 3, Ga.

ILLINOIS

First Medical Students' Loans.—Three premedical students have received loans of $5,000 to finance their medical education under the $100,000 joint medical student loan fund set up by Illinois Agricultural Association and the Illinois State Medical Society. The students and the universities which they will attend are: Burton E. Bagby of Mounds, Loyola University Stritch College of Medicine, Chicago; L. C. Fiene of Sparta and Lawrence Irish of Blandensville, the University of Illinois. Men from rural communities who have completed premedical courses, who are approved by local farm bureaus and medical societies and who will agree to practice in rural communities are eligible for $5,000 loans at the rate of $1,000 a year to complete their four year medical courses and one year internships. A list of twenty priority counties, where the situation is worse than usual, has been set up for Illinois. All three candidates are from such counties. The scholarship loan plan for medical training was established late in 1947 (THE JOURNAL January 1, page 48).

Chicago

Belfield Memorial Lecture.—The Chicago Urological Society at its meeting October 21 will hear the annual William T. Belfield Memorial Lecture, by Dr. Charles P. Mathe of San Francisco on "Operative Interventions on the Solitary Kidney." All society meetings for the year will be held in the Congress Hotel.

Symposium on Medicolegal Problems.—A symposium on Medico-Legal Problems will be held on Tuesday evenings at 7:30 October 26 through November 23 and on December 2 at the Chicago Bar Association. The programs, under the sponsorship of the Institute of Medicine of Chicago, the Chicago Medical Society and the Chicago Bar Association, are as follows:

Oct. 26, Mental and Chronological Age Problems in Law and Medicine: Medical Presentation, David Shakow, Ph.D., Chicago; Legal Presentation, Hon. Joseph J. Drucker, Chicago.
Nov. 2, Sex Offenses and Sex Offenders: Medical Presentation, Harry R. Hoffman, Chicago; Legal Presentation, Erwin W. Roemer, Esq., Chicago.
Nov. 9, Modern Methods of Crime Detection: Medical Presentation, Roy R. Grinker and Mr. Leonard Keeler, Chicago; Legal Presentation, Fred E. Inbau, Esq., Chicago.
Nov. 16, Income Tax Discrimination Against the Professions: Medical Presentation, Frank G. Dickinson, Ph.D., Chicago; Legal Presentation, Robert P. Spindell, Esq., Chicago.
Nov. 23, Problems of Alcoholism from the Medical and Industrial Aspects: Medical Presentation, Andrew C. Ivy, Chicago; Industrial Aspects: Edward C. Holmblad, Chicago; Legal Presentation, James J. McKenna, Esq., Chicago.
Dec. 2, How Can the Constitutional Office of Coroner Serve Modern Needs: Medical Presentation, Herbert S. Breyfogle, Richmond, Va.; Legal Presentation, Francis X Busch, Esq., Chicago.

New Radio Health Series.—The Chicago Industrial Health Association will inaugurate its radio health series, entitled "It's Your Life," on October 18, at 11:15 to 11:30 a. m. over station WMAQ. The program, sponsored by Johnson and Johnson, will provide stories of better living through authentic tape-recorded interviews with anonymous Chicagoans. The plan is to include all phases of personal, family, community and industrial health. About 300 of Chicago's health and welfare agencies will aid with the planning and production of the programs. Broadcasts will be outlined by the association's radio advisory committee, composed of medical authorities, and will be completely reviewed by the committee and the educational committee of the Illinois State Medical Society. The Chicago Industrial Health Association was organized last January as a joint undertaking by the city officials and voluntary health and medical agencies, business and labor organizations and industrial and commercial firms. It is planning an extended program to include the community as a whole through the following health services: a health and social welfare referral service for employees, a monthly news letter to management, health agency surveys and services for industry, and a panel of leading industrial physicians and surgeons to assist firm medical departments.

Dr. Miller Elected President of Northwestern University.—Dr. J. Roscoe Miller, dean of Northwestern University Medical School, has been elected president of Northwestern University and will assume office July 1, 1949. He succeeds Franklyn B. Snyder, who will retire Sept. 1, 1949. Dr. Miller will be the twelfth president of the university. Dr. John Evans, the founder and first president of the university, also was a physician and medical educator. Dr. Miller, a native of Utah, has been a member of the teaching staff of Northwestern University Medical School since 1930, in which year he received his M.D. degree from Northwestern. He served as assistant dean of the school from 1933 until his appointment as dean in 1941. During World War II he was a commander in the Medical Corps, U. S. Navy, in charge of the section on internal medicine of the Professional Division, Bureau of Medicine and Surgery, Washington, D. C. Dr. Miller is now president of the Chicago Medical Society, president elect of the Association of American Medical Colleges, a trustee of Wesley Memorial and Passavant Memorial and Evanston hospitals, and a member of numerous medical societies and associations. Under his able guidance during the past seven years the medical school has made outstanding progress in teaching and research and has increased its facilities and assets.

INDIANA

State Association News Letter.—The first issue of the Indiana State Medical Association's monthly *News Letter* was published in August as a supplement to the journal. It will be sent to all members of the state association.

Dr. Huber to Head Department.—Dr. Carl P. Huber, associate professor of obstetrics and gynecology, Indiana University School of Medicine, Bloomington-Indianapolis, was made professor and chairman of the new department of obstetrics and gynecology at the university August 1. Dr. Huber is a graduate

of the University of Michigan Medical School, Ann Arbor, 1928. He has been a staff member of the medical school and university hospitals at the medical center for nearly ten years. He also serves as consultant in obstetrics to the Indiana State Board of Health.

KANSAS

Society News.—At a meeting June 19 in Wichita, the Kansas Psychiatric Society chose Dr. Jesse F. Casey, Topeka, as president, and Dr. Frank F. Merker, Topeka, secretary-treasurer.

Postgraduate Course.—Menninger Foundation School of Psychiatry and the Winter Veterans Administration Hospital in Topeka are accepting applications for admission to the school on Jan. 1, 1949, available only to doctors who have had some psychiatric residency training in an approved hospital and who can therefore qualify for advanced standing. Those accepted will be placed in the class which entered July 1, 1948. Application should be made to Dr. Bert Boothe, Director of Professional Education, Winter VA Hospital, Topeka, Kansas.

MASSACHUSETTS

Public Health Forums at Harvard.—The second Public Health Forum of the Harvard University School of Public Health will be held at the school October 14 at 3:30 p. m. Dr. James R. Miller, Hartford, Conn., member of the executive committee of the Board of Trustees of the American Medical Association, will speak on "Opportunities Presented by the Development of National Health Program for the Public Health Profession and Private Practitioners of Medicine to Coordinate Their Activities in the Public Interest." The third forum speaker, Dr. Morris Fishbein, Editor of THE JOURNAL, will speak on November 16, at 3:30 p. m., on "Trends in Social Security."

Personals.—Dr. Harlan L. Paine, North Grafton, resigned as superintendent of the Grafton State Hospital, September 15, after completing twenty-seven years' service, to assume the superintendency of the Channing Sanitarium, Inc., in Wellesley. Dr. Paine served the department of mental health of the Commonwealth of Massachusetts for thirty-nine years.——Boston University School of Medicine has appointed Colonel Charles B. Perkins, Medical Corps, United States Army, as instructor of Army medical and military science and professor of radiology. Colonel Perkins is now serving as a resident in radiology at Massachusetts Memorial Hospitals under Dr. George Levene, chief of radiology.

MICHIGAN

The Biddle Lecture.—Dr. Edward A. Strecker, professor of psychiatry at the University of Pennsylvania School of Medicine, Philadelphia, presented the Biddle Lecture at the annual session of the Michigan State Medical Society September 22, on "Compromise or Chaos."

Hearing Consultants Service.—Schools in fifty counties have requested the service of the Michigan Department of Health's two hearing consultants this year. More than 250,000 children have been examined for hearing loss since the department's program began in 1943. Of the 3 per cent showing some hearing loss, about 50 per cent improved to normal hearing, according to the state department of health.

Survey of Premature Babies' Deaths.—The Bureau of Maternal and Child Health of the Michigan Department of Health is conducting a survey of the causes of death of babies born prematurely and is urging all expectant mothers to get early medical care. The bureau estimates that 8,000 premature infants were born in Michigan last year and, according to the death certificates, more than half of the 5,120 infant deaths were from causes related to prematurity. Pamphlets to aid the expectant mother may be obtained from local health departments or from the Michigan Department of Health, Lansing 4.

MINNESOTA

Receives Hospital Association Award.—Mr. James A. Hamilton, director of the hospital administration course at the University of Minnesota, Minneapolis, received the Award of Merit of the American Hospital Association for many years of leadership and activity in behalf of hospitals and the association. The award was conferred at the association meeting in Atlantic City, N. J., September 20-23.

Clinical Conference.—The Fall Clinical Conference of the Wells County Medical Society was conducted at the Bluffton Country Club September 15. Guest speakers were:

Fred L. Adair, Chicago, Toxemias of Pregnancy.
Archibald L. Hoyne, Chicago, Poliomyelitis Problems.
Frederick B. Wishard, Anderson, Ind., Routine Chest Surveys in Industry.
James O. Ritchey, Indianapolis, Ind., Dyspnea of Cardiac Origin.

NEW YORK

Historical Portrait.—The Westchester County Medical Society has been presented an oil portrait of one of its early members, Dr. Isaac G. Graham, who was an assistant surgeon in the American army during the Revolutionary War and served under General Washington at West Point. The portrait was presented to the society by Mrs. F. Worden M. Graham, Washington, D. C., at the wish of her recently deceased husband, a great grandson of Dr. Isaac Graham. Dr. Isaac Graham began his medical practice in Unionville (now Hawthorne) in 1784 and continued in active practice for over half a century. He died September 1848, aged 88.

Postgraduate Instruction.—The Medical Society of the State of New York with the cooperation of the New York State Department of Health has arranged the following postgraduate lectures: The Richmond County Medical Society meeting at the Old Mill, Staten Island, November 10, at 9:30 p. m., will hear Dr. Howard C. Taylor Jr., New York, speak on "Physiologic Studies of Toxemia of Pregnancy." On December 8 they will hear a symposium on "Heart Disease and Pregnancy" given by two Brooklyn doctors, Edwin P. Maynard Jr. and Thornton Wallace. On November 2 Dr. George P. Heckel, Rochester, will speak on "Practical Application of Endocrines in Gynecology" before the members of the Schenectady County Medical Society, meeting in the auditorium of the Eastern New York Orthopedic Hospital, Schenectady, at 8:30 p. m.

New York City

Dr. Snyder to Direct Clinic.—Dr. Joseph E. Snyder has been named director of the Vanderbilt Clinic, the outpatient department for the voluntary hospitals of the Columbia-Presbyterian Medical Center, and administrative assistant in charge of the Columbia-Presbyterian Medical Center and of professional services to patients at the clinic. Dr. Snyder is a graduate of the University of Pennsylvania School of Medicine, Philadelphia, 1943.

Personals.—Dr. Martin R. Steinberg, assistant director since 1945, has been appointed director of Mount Sinai Hospital of New York, succeeding Dr. Joseph Turner, who has been named consultant to the Board of Trustees.——Dr. Edward L. Howes, associate clinical professor of surgery, Columbia University College of Physicians and Surgeons, was recently made an honorary member of the Piedmont Surgical Society of Northern Italy.

Reading Program for Mentally Ill.—Columbia University's School of Library Science is conducting a study "to develop the basic types of reading programs" that may aid mentally ill patients. A special internship has been established at a state hospital in the metropolitan area and a qualified graduate librarian is working under the direction of the hospital. A course entitled "library work with hospital patients" has been established to aid this work. The program is designed to determine whether rehabilitation is stimulated or retarded through planned reading programs.

OHIO

University Retirements.—Dr. Arthur H. Bill, Cleveland, retired in June as head of the obstetrical department of Western Reserve University School of Medicine. He expects to continue his private practice. Dr. Morse F. Osborn, a member of the Ohio State University College of Medicine Student Health Staff, Columbus, for twenty years, retired this summer.

Dr. Alter Goes to Beirut.—Dr. Robert L. Alter, Toledo, will assume duties in October as professor and head of the department of obstetrics and gynecology at American University in Beirut, medical center of the Near East. En route he will lecture in Munich, Germany, before displaced doctors in a program arranged by the International Refugee Organization, a branch of the United Nations. Dr. Alter received his medical degree in 1937 from Duke University School of Medicine, Durham, N. C., where he later became an instructor in obstetrics and gynecology. In 1946 he moved to Toledo, where he engaged in private practice.

PENNSYLVANIA

Personal.—Dr. John B. F. Wyant has resigned as medical examiner in Kittanning and rural public schools after having served nearly sixty years. The school directors, on accepting his resignation, named him a lifetime honorary physician of the local school district.

Graduate Course in Cancer.—The School of Medicine of the University of Pennsylvania, Philadelphia, will present three courses this year in the diagnosis and treatment of cancer for physicians, under a grant from the State Department of Health. The first course will extend from November 8 to 20; the second

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from January 17 to 29, 1949, and the third, April 25 to May 6, 1949. The courses are limited to small groups. Application must be received not later than four weeks before the opening date of the courses applied for. Application blanks will be sent on request to Dr. Robert C. Horn, Secretary of the Cancer Commission, Hospital of the University of Pennsylvania, Philadelphia 4. Tuition fees and some compensation for time spent away from regular practice will be paid by the Division of Cancer Control of the State Health Department.

Pittsburgh

Dr. Parran to Head New School of Public Health.—A new graduate school of public health is being set up at the University of Pittsburgh through a $13,600,000 grant from the A. W. Mellon Educational and Charitable Trust. The first dean of the new school will be Dr. Thomas Parran, former Surgeon General of the United States. The school will emphasize occupational and industrial health and hygiene and do basic research in all phases of public health. It is expected that the school will begin operation by the fall of 1949. An initial $4,000,000 will enable the university to obtain an adequate faculty and facilities for teaching, and $1,600,000 will be given during the first five years for operating and equipment expenses and for development. A $5,000,000 building to house the school will be erected as soon as the school is accredited and the university is able to integrate its medical schools and hospitals in the medical center. The final $3,000,000 will be paid within five years, when the school has developed "into a successful undertaking." Dr. Parran is a graduate of Georgetown University School of Medicine, Washington, D. C. He joined the public health service in 1917 and in 1936 began the first of three terms as Surgeon General. From 1930 to 1936 he was commissioner of health for New York State. Since early in 1948 he has served as chief of a mission to the Far East for the United Nations International Childrens Emergency Fund. His most recent assignment was chairman of the U. S. delegation to the first World Health Organization meeting in Geneva, Switzerland, June-July, 1948.

SOUTH DAKOTA

University Appointments.—Recent appointments to the University of South Dakota School of Medical Sciences, Vermillion, include: Dr. Thomas E. Eyres, professor of public health and director of student health; assistant professors, Dr. Jacob B. Belogorsky, pharmacology; Harold M. Carlisle, Ph.D., microbiology; Dr. James Y. Clarke, clinical pathology and parasitology, and Robert H. King, Ph.D., biochemistry; clinical associate professor, Dr. David J. Tschetter, radiology; assistant clinical professors, Drs. Brooks Ranney, obstetrics and gynecology, and Theodore H. Sattler, medicine; research assistant professor of oncology, Dr. Francis C. Tucker; associates, Keatha K. Krueger, Ph.D., biochemistry, and Dr. Theodore T. Mazur, anatomy; Kenneth R. Berquist, M.A., instructor in microbiology. Drs. E. M. Stansbury and Harold F. Hansen were promoted to clinical associate professors of obstetrics and gynecology and physical diagnosis, respectively.

WASHINGTON

Dr. Ripley Appointed Head of the Department of Psychiatry.—Dr. Herbert S. Ripley, assistant professor of psychiatry at Cornell University Medical College, New York, has been appointed professor of psychiatry and executive officer of the department of psychiatry at the University of Washington School of Medicine, Seattle. Dr. Ripley obtained his M.D. degree at Harvard Medical School, Boston, 1933. He has served on the staff of the New York Hospital and has been assistant, instructor and assistant professor in psychiatry, all at Cornell. Following his service during World War II, he served as consultant in psychiatry for the Veterans Administration and since 1947 has been consultant in psychiatry for the U. S. Public Health Service.

WISCONSIN

Personal.—The Biological Photographic Association recently gave its first annual award to Leo C. Massopust, director of the department of art and photography, Marquette University School of Medicine, and editor of the association's journal.

Dedicate Coolidge Laboratory.—Dedication ceremonies for the William D. Coolidge Laboratory of the General Electric X-Ray Corporation, Milwaukee, were held at the laboratory September 13. Among the speakers were Dr. Arthur C. Christie, Washington, D. C., who spoke on "Contributions of Industrial Research to Medicine." William D. Coolidge, Ph.D., who retired in 1944 as vice president and director of research of the General Electric Company, spoke on "Highlights of the Past and a Challenge for the Future." Charles E. Wilson, president, General Electric Company, was speaker at the dinner.

HAWAII

Personal.—Dr. Robert H. Marks, chief of the Tuberculosis Bureau of the Territorial Department of Health, Honolulu, has resigned to return to the mainland as medical director of Jefferson Tuberculosis Sanatorium, Birmingham, Ala.

Health Department Appointments.—Dr. Angie Connor, recently associated with the Children's Heart Association in Cincinnati, began duties July 1 as clinical pediatrician in the Bureau of Maternal and Child Health and Crippled Children. She is a graduate of Woman's Medical College of Pennsylvania, Philadelphia, 1937. Dr. Yan Tim Wong assumed duties July 1 as assistant chief and child psychiatrist with the Bureau of Mental Hygiene. He is a graduate of Peiping Union Medical College, China, where he served as assistant physician in neuropsychiatry.

PUERTO RICO

Foreign Physicians Wanted.—Governor Jesus T. Piñero of Puerto Rico has signed a bill appropriating the sum of $80,000 to contract the services of physicians in the United States and foreign countries to be employed in the municipal hospitals of the island where there is a shortage of doctors. Such physicians must sign a contract to serve with the Insular or Municipal governments of Puerto Rico, in accordance with conditions stipulated by the Commissioner of Health. According to Governor Piñero the 1947 mortality rate in Puerto Rico was 12.50 persons per thousand population, compared with 14.1 per cent in 1945. Infant mortality, which was of 39.5 in 1945 per thousand, dropped to 17.5 in 1947. The death rate for tuberculosis which was 202.5 per 100,000 inhabitants in 1945, dropped to 196.7 in 1947. Victims of malaria in 1945 were 43.1 per 100,000 population against 20.0 in 1947.

GENERAL

Society Election.—At the recent meeting of the Harvey Cushing Society Dr. Winchell McK. Craig, Rochester, Minn., was elected president; Dr. Howard A. Brown, San Francisco, vice president, and Dr. Louise C. Eisenhardt, New Haven, Conn., secretary-treasurer.

International College of Surgeons.—The Annual Assembly and Convocation of the United States Chapter, International College of Surgeons, will be held at the Kiel Auditorium, St. Louis, November 16-19. The program of scientific sessions will be supplemented by operative and nonoperative clinics in hospitals in St. Louis and vicinity. Extensive technical and commercial exhibits and motion pictures are scheduled.

Meeting of Public Health Association.—The annual meeting of the American Public Health Association and its twenty-nine related organizations will be held in Mechanics Hall, Boston, November 8-12. More than three hundred papers will be presented before the association's twelve sections: Dental health, engineering, epidemiology, food and nutrition, maternal and child health, health officers, industrial hygiene, laboratory, public health education, public health nursing, school health and vital statistics.

Grant by American Heart Association.—A $25,000 grant from The American Heart Association has been presented to the Szent Gyorgyi Research Foundation, to aid studies in muscular contraction being conducted at the Marine Biological Institute, Woods Hole, Mass. The grant is the first in a program of financial assistance to heart disease research, which the association has been enabled to undertake as a result of its initial nationwide fund-raising campaign earlier this year. Dr. Szent Gyorgyi is director of research for the foundation, incorporated this year to aid scientific and educational research.

Southern Medical Association.—This association will convene in Miami, Fla., October 25-28 with headquarters at Dinner Key. The program will open with three general sessions which include a panel discussion on anticoagulant therapy and cardiovascular disease with Dr. E. Sterling Nichol, Miami, moderator, and another on peripheral vascular disease with Dr. George D. Lilly, Miami, moderator. The remaining program is divided into numerous sections on the specialties. The president's reception and ball will be held at the Municipal Auditorium in Bayfront Park October 27. The Woman's Auxiliary will meet in conjunction with the association.

Tuberculosis Death Rate Higher for Men.—According to the U. S. Public Health Service, tuberculosis statistics for the past thirty-seven years show that the death rate from tuberculosis in the United States is nearly twice as great for men as for women. During this period the death rate for the disease in the country as a whole has declined from 153.8 to 36.4 per year per 100,000 population. At the beginning of the period the death rate for both white and nonwhite males was about one-fifth higher than the rate for females, but in 1946 there was a

difference of more than 90 per cent between white men and white women. Among the colored population the death rates were 34 per cent higher for males than for females.

Improved Cancer Mortality Among Women.—Decline in the mortality from cancer, including the leukemias and Hodgkin's disease, among women insured in the Industrial Department of the Metropolitan Life Insurance Company has continued almost without interruption from 93.5 per 100,000 in 1932-1934 to 82.9 in 1947. These encouraging trends are attributed to the persistent campaign in popular education regarding cancer, which has resulted in women's seeking medical attention earlier, when the chances of cure are more favorable. Patients who had delayed three months or more decreased from 62.3 per cent of the total from 1923 to 1938 to 42.8 per cent in 1946. In contrast, the recorded death rate from cancer among white females at 1 to 24 years rose from about 5 per 100,000 in 1932-1934 to 6.8 per cent in 1945-1947. The study was published in the *Statistical Bulletin* in August.

Incidence of Poliomyelitis.—The U. S. Public Health Service reported September 22 that 1,841 cases of poliomyelitis were reported for the previous week. In general the incidence declined in the Southern states but increased in the Northern states and in California. Increases aggregating 381 cases were reported as follows: California, 205 to 326; Ohio, 79 to 149; South Dakota, 10 to 55; Illinois, 71 to 99; Tennessee, 13 to 38; Pennsylvania, 51 to 74; New Jersey, 50 to 71; New York, 95 to 115; Minnesota, 101 to 115, and Michigan, 57 to 71. The most important decreases were reported in South Carolina, from 112 to 76; Texas, from 57 to 42; West Virginia, from 28 to 10, and Oklahoma, from 37 to 19. Total cases reported through the week ended September 18 was 16,029, as compared with 5,617 in 1947, 15,780 in 1946, and a five year median of 8,009 for the corresponding periods.

Mental Hygiene Committee.—The annual meeting of the National Committee for Mental Hygiene will be held on November 3-4 at the Hotel Pennsylvania, New York. The program will consist of four scientific sessions during the mornings and afternoons, a business luncheon on the first day and the annual luncheon on the second day, at which the presentation of the Lasker Award will be made and the ten year national program for mental health discussed. The first scientific session will be devoted to international matters emerging from the International Congress on Mental Health held August 11-21 in London, the program of UNESCO and the World Health Organization and the newly organized World Federation for Mental Health. The second session will be a current evaluation of the federal mental hygiene program. The third session will focus on the development and responsibility of the citizen for improvement of the state psychiatric services, and the fourth session will clarify the foundations for positive mental health and the activities supportive of this goal.

Grants for Research.—The Jane Coffin Childs Memorial Fund for Medical Research has announced a total of $84,275 for support of cancer research projects and fellowships. Among the grants were $4,100 for one year to Dr. William B. Atkinson, assistant professor of anatomy, and Dr. Howard C. Taylor Jr., professor of obstetrics and gynecology, Columbia University College of Physicians and Surgeons, New York, for cytochemical investigations on hyperplastic and malignant uterine tissues in women in relation to their endocrine state; $15,000 for three years to Edward L. Tatum, Ph.D., Stanford University School of Medicine, San Francisco, for studies on gene mutation in micro-organisms in relation to enzyme production and activity, and $5,000 for one year to Dr. Gray H. Twombly, assistant professor of clinical obstetrics and gynecology, Columbia University College of Physicians and Surgeons, New York, for a study of selective localization of hormones in normal and cancer-bearing tissues by radioactive estrogens and allied substances.

New Cancer Journal.—A monthly journal, *Cancer*, devoted exclusively to cancer, with major emphasis on clinical reports and experimental studies, appeared in May of this year. In addition to the original papers, it includes a complete current bibliography of the world-scattered literature on cancer, as well as abstracts of all significant papers. The journal, sponsored by the American Cancer Society, contains no paid advertising, has an attractive format and is liberally illustrated. The editor is Dr. Fred W. Stewart, New York. The editorial advisory board is made up of forty-four leaders in the study and treatment of cancer and seven authorities on education and public health statistics. The first issue was dedicated to the memory of Dr. James Ewing (1866-1943), American pioneer in neoplastic diseases. Subscriptions and business inquiries should be addressed to the publisher, Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 49 East 33rd Street, New York 16. Contributions should be addressed to the editor, Memorial Hospital, 44 East 68th Street, New York 21.

Interim Report of the National Foundation.—The National Foundation for Infantile Paralysis in its 88 page interim annual report published early in September showed that a total of $4,675,971 in March of Dimes funds was allocated to poliomyelitis research, education and epidemic aid during the seven month period ending Dec. 31, 1947. The report announced that $474,827 was spent on virus research, $254,480.13 in research on prevention and treatment of after-effects, $160,000 for medical care, $1,022,045.96 for professional education and $2,764,618.30 for emergency epidemic aid. In the past five years 81,530 cases of poliomyelitis have been reported as compared with 31,993 in the previous five year period. Nationally, epidemics of 1947 showed a total of 10,734 cases as compared with 25,698 in 1946. In 1947 three states, Ohio, Idaho and Delaware, suffered their most severe epidemics of poliomyelitis. In professional education the National Foundation has spent $4,382,994 in the last decade on advanced training for nurses, physical therapists, orthopedists, pediatricians, neurologists and other specialists; a parallel program has been carried on to educate and inform the public.

The World Health Assembly.—Representatives and observers from sixty-eight nations met at Geneva, Switzerland, June 24 to July 24, to form the permanent structure of the World Health Organization. Of fifty health activities considered, priority was given to global campaigns against malaria, tuberculosis, venereal infections and the promotion of maternal and child welfare, better nutrition and environmental hygiene. Work is being continued by the World Health Organization in international epidemiology and quarantine; health statistics and nomenclature; fellowships, medical literature and emergency services. International standards, including therapeutic, prophylactic, diagnostic agents, the international pharmacopeia, editorial services and publications, including reference services and library, were also considered.

Dr. Brock Chisholm of Canada was elected the World Health Organization's first director-general. Prior to becoming executive secretary of the Interim Commission of the World Health Organization in 1946, Dr. Chisholm had served since November 1944 as Canada's first Deputy Minister of Health. The appointed, eighteen member, executive board met under the chairmanship of Sir Aly Tewfik Shousha Pasha, Egypt.

Budgets of $4,800,000 for the rest of 1948 included repayment of a $2,000,000 loan from United Nations; $5,000,000 was approved for 1949. At the invitation of the Pasteur Institute of Paris, the World Health Organization will make use of its many laboratories throughout the world in studying epidemiologic diseases.

CORRECTION

Artificial Kidney.—In the article of this title by Gordon Murray and co-workers in THE JOURNAL Aug. 28, 1948, table 2, page 1397, the last chemical mentioned in the formula should be "sodium bicarbonate" and not "sodium carbonate."

Marriages

JACK WHITE MCELWAIN, Syracuse, N. Y., to Miss Ruth Van Deventer Jones at Locust Valley, L. I., June 12.

ROBERT BEEBE PENDER, Utica, N. Y., to Miss Alice Culpepper Gordon of Daytona Beach, Fla., June 12.

WILLIAM CECIL BAKER, Williamsville, N. Y., to Miss Dorothy Louise Herron of Five Mile, June 19.

JAMES ENGLISH COUSAR III to Miss Mary Evelyn Young, both of Florence, S. C., June 19.

ROBERT WHEARY IRVIN JR., Roanoke, Va., to Miss Dorothy Louise McGee of Ford, June 21.

JAMES EDWARD RYAN to Miss Mary Margaret Douglas, both of Schenectady, N. Y., June 12.

HARRY C. FOSTER JR., Richmond, Va., to Miss Billie Newton of Charlotte, N. C., June 26.

JOSEPH E. MOLLOY, Hilo, Hawaii, to Miss Ruth W. Hopton of Marseilles, Ill., June 9.

JOHN EDWARD DAVIS JR., to Miss Janet Edith Hannon, both of Troy, N. Y., May 15

WILLIAM FRANK to Miss Betty Rose Smith, both of Washington, D. C., recently.

WILLIAM F. HEGGLI, San Francisco, to Miss Lucille Hotto at St. Louis, recently.

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Deaths

John Aikman ● Rochester, N. Y.; born in Roxbury, N. Y., Jan. 12, 1885; University and Bellevue Hospital Medical College, New York, 1908; assistant professor of pediatrics at the University of Rochester School of Medicine and Dentistry; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; past president of the Rochester Academy of Medicine which in 1948 awarded him the Albert David Kaiser Medal for outstanding medical service; chairman of the Section on Pediatrics of the American Medical Association from 1944 to 1946; served during World War I; affiliated with the Strong Memorial, Park Avenue, Genesee and Rochester General hospitals; died July 13, aged 63, of cerebral thrombosis.

Leo Winter, New York; born in New York, May 26, 1890; University and Bellevue Hospital Medical College, New York, 1934; also a dentist; professor of oral surgery and director of the oral and minor surgery clinic, New York University College of Dentistry; member of the American Medical Association; fellow of the American College of Surgeons; served in France during World War I; consulting oral surgeon, Montefiore Hospital for Chronic Diseases; visiting dental surgeon, Bellevue and New York Foundling hospitals; author of "A Textbook of Exodontia" and "Operative Oral Surgery"; an honorary medical officer of the fire department; died in Lawrence, Long Island, July 6, aged 58, of heart disease.

Frank John Novak Jr., ● Chicago; born in Chicago, July 3, 1888; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1914; specialist certified by the American Board of Otolaryngology; member of the American Laryngological, Rhinological and Otological Society and the American Otological Society; in 1948 received a gold medal from the American Academy of Ophthalmology and Oto-Laryngology for his many years' service to the academy; served during World War I; lieutenant colonel, medical corps, Army of the United States, not on active duty; on the staff of the Henrotin Hospital; died at Riverside, Ill., July 27, aged 60, of coronary sclerosis.

J. Wilford Allen, South Kent, Conn.; New York Homeopathic Medical College and Hospital, New York, 1895; served on the faculty of his alma mater and a member of the Connecticut Homeopathic Medical Examining Board; formerly on the staffs of the Hahnemann and Flower hospitals in New York; died in the Charlotte Hungerford Hospital in Torrington, July 17, aged 83, of fracture of the neck of the femur and arteriosclerotic heart disease.

Edward Lawrence Asbell ● Kansas City, Kan.; St. Louis College of Physicians and Surgeons, 1896; affiliated with Providence, Bethany and St. Margaret's hospitals; died July 3, aged 75, of heart disease.

Zae R. AschenBrenner ● Farmington, Mich.; State University of Iowa College of Medicine, Iowa City, 1920; past president of the Oakland County Medical Society; served during World War I; for many years president of the school board; died in the Harper Hospital, Detroit, July 20, aged 55, of acute lymphatic leukemia.

Paul Herbert Bishop Jr., Coraopolis, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1943; interned at the Williamsport Hospital in Williamsport; formerly resident at the Veterans Administration Hospital in Memphis, Tenn.; served during World War II; died July 5, aged 30.

Ernest Lehman Wheeler Brown, Iowa Falls, Iowa; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; member of the American Medical Association; veteran of the Spanish-American War; died July 19, aged 73.

Frederic Bushong ● Pottstown, Pa.; Jefferson Medical College of Philadelphia, 1907; died April 15, aged 68, of chronic rheumatic heart disease.

Alexander McConnal Butts, Holdenville, Okla.; Vanderbilt University School of Medicine, Nashville, Tenn., 1895; died July 2, aged 77.

James Graham Calhoun, St. Louis; Washington University School of Medicine, St. Louis, 1896; specialist certified by the American Board of Ophthalmology; member of the American Medical Association and American Academy of Ophthalmology and Otolaryngology; served during World War I; died in Deaconess Hospital July 5, aged 79, of subarachnoid hemorrhage and hypertension.

Robert E. L. Campbell ● Baltimore; University of Maryland School of Medicine, Baltimore, 1904; also a graduate in pharmacy; died in the Maryland General Hospital June 30, aged 73, of bronchopneumonia and carcinoma of the stomach.

C. Gray Capron ● Utica, N. Y.; Hahnemann Medical College and Hospital of Philadelphia, 1890; surgeon in chief at the Commercial Travelers Mutual Accident Association; died in Cooperstown, July 10, aged 81, of coronary thrombosis.

Clarence A. Carpenter ● Onaway, Mich.; Physio-Medical College of Indiana, Indianapolis, 1898; first president of the Presque Isle County Medical Society; formerly health officer of Onaway; died in Little Traverse Hospital, Petoskey, July 17, aged 73, of carcinoma of the stomach with metastases to the liver.

Rodolph Kossuth Comeaux, Youngsville, La.; University of the South Medical Department, Sewanee, Tenn., 1903; died June 12, aged 69.

William Cornelius Couch, St. Petersburg, Fla.; Gross Medical College, Denver, 1895; member of the American Medical Association and the Medical Society of the State of New York; formerly practiced in Watertown, N. Y., where he was on the staffs of the House of the Good Samaritan and Mercy Hospital, where he died July 5, aged 78, of carcinoma of the stomach.

Reuben Cronson ● New Rochelle, N. Y.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1888; a founder and past president of the medical board of Jewish Memorial Hospital in New York; died in Miami Beach, Fla., July 4, aged 87, of myocardial failure.

Percy Edwin Decatur, Ashland, Ohio; Eclectic Medical College, Cincinnati, 1904; member of the American Medical Association; served during World War I; member of the staff of Samaritan Hospital; died May 30, aged 73, of injuries received in a fall.

Enos Goble Denison ● Sheridan, Wyo.; Ohio Medical University, Columbus, 1903; past president of the Wyoming Department of Public Health; served during World War I; on the staff of Sheridan County Memorial Hospital; division surgeon for the Chicago, Burlington and Quincy Railroad; died May 12, aged 73, of coronary thrombosis.

Clifford Ferrins Dowhontt, New York; Yale University School of Medicine, New Haven, 1919; died July 13, aged 55.

Charles Daniel Eby ● Leigh, Neb.; University of Nebraska College of Medicine, Omaha, 1904; died in Lutheran Hospital, Omaha, July 28, aged 69, of cerebral embolism.

Edward Hollinger Epler, Philadelphia; Medico-Chirurgical College of Philadelphia, 1910; died May 6, aged 73, of acute coronary occlusion.

Fred Franklin Farr, Neelsville, Mo.; Barnes Medical College, St. Louis, 1898; died June 28, aged 70.

Charles Wilmer Fitch, New York; Columbia University College of Physicians and Surgeons, New York, 1899; member of the American Medical Association; died July 1, aged 74, of arteriosclerotic heart disease.

Zenobia Gustava Gilpin, Richmond, Va.; Howard University College of Medicine, Washington, D. C., 1923; on the staff of Richmond Community Hospital; served on the city lunacy commission; died June 11, aged 48.

Oswald Glasberg, New York; Medizinische Fakultät der Universität, Wien, Austria, 1926; member of the American Medical Association; died July 15, aged 49.

Onslow Allen Gordon ● Brooklyn; Long Island College Hospital, Brooklyn, 1911; formerly clinical professor of obstetrics and gynecology at the New York University College of Medicine; served during World War I; fellow of the American College of Surgeons; fellow and past president of the New York Obstetrical Society and the Brooklyn Gynecological Society; affiliated with the Carson C. Peck Memorial Hospital; consultant in obstetrics at St. John's Hospital; died July 7, aged 61, of carcinomatosis.

Harry Hinshillwood, Danville, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1895; died recently, aged 79, of cerebral thrombosis and hypertension.

Allen Webb Hobby, Sidney, Ohio; Eclectic Medical Institute, Cincinnati, 1899; died recently, aged 71, of cerebral hemorrhage.

Robert Edward Hogan ● West Plains, Mo.; Washington University School of Medicine, St. Louis, 1909; member of the school board; president of the West Plains Bank; owner of the Christa Hogan Hospital; died in Missouri Baptist Hospital, St. Louis, July 8, aged 60, of pneumonia, following an operation.

Henry Lincoln Houghton, Boston; Harvard Medical School, Boston, 1894; member of the American Medical Association; at one time member of the board of registration in medicine; during World War I head of the medical examining board for the draft in Boston; past president of the Hahnemann Hospital; died June 17, aged 80, of arteriosclerotic heart disease.

Mortimer A. Houser ● Tulsa, Okla.; Milwaukee Medical College, 1903; for many years official examiner for the city athletic commission; died in Bentonville, Ark., June 20, aged 70, after an operation.

Charles Bartholomew Howard, Philadelphia; Howard University College of Medicine, Washington, D. C., 1922; died June 7, aged 59, of heart disease.

William L. Howard, Western State Hospital, Tenn.; Memphis (Tenn.) Hospital Medical College, 1895; member of the American Medical Association; specialist certified by the American Board of Otolaryngology; assistant physician at Western State Hospital; died in Campbell's Clinic, Memphis, July 3, aged 76, of embolism, following a fractured hip received in a fall.

John David Howland, Cheektowago, N. Y.; Niagara University Medical Department, Buffalo, 1891; served during the Spanish-American War and in France during World War I; formerly deputy medical examiner for Erie County; for many years associated with the Erie County Home and Infirmary in Buffalo; died in Buffalo General Hospital June 16, aged 83, of carcinoma.

Clarence Elmer Hyde, San Francisco; Columbia University College of Physicians and Surgeons, New York, 1909; member of the American Medical Association; died in San Jose, June 6, aged 66, of bronchopneumonia and arteriosclerosis.

Lucia Kemp, Bucyrus, Ohio; Fort Wayne College of Medicine, 1891; died June 24, aged 85.

Lester Floyd Kennedy ● Detroit; Detroit College of Medicine and Surgery, 1915; died June 28, aged 56.

Ralph William Kraft ● Hobart, Ind.; Indiana University School of Medicine, Indianapolis, 1936; at one time assistant superintendent of the Ohio State Sanatorium in Mount Vernon; member of the staffs of Mercy and Methodist hospitals in Gary and Porter Memorial Hospital in Valparaiso; served as health commissioner and school physician; accidentally shot and killed in a hunting lodge near Ely, Minn., June 23, aged 38.

Harry Lee, Waterhill, Tenn.; University of Tennessee Medical Department, Nashville, 1900; died May 20, aged 73, of nephritis and myocardial insufficiency.

Joseph Ira Lindsay, Grafton, Mass.; University of Vermont College of Medicine, Burlington, 1888; member of the American Medical Association; formerly on the staff of Memorial Hospital, Worcester; died June 6, aged 85.

Herbert Milton Long ● Pittsburgh; University of Pittsburgh School of Medicine, 1914; fellow of the American College of Surgeons; chief surgeon for the Pittsburgh and Lake Erie Railroad; served during World War I; member of the staff of the Southside Hospital; died June 15, aged 58, of sarcoma.

Frederick Henry Lovell, Irvington, N. J.; the Hahnemann Medical College and Hospital, Chicago, 1909; served on the staff of the Irvington General Hospital, where he died July 6, aged 87, of arteriosclerosis.

James Chalmers Lyons, Linwood, Pa.; Jefferson Medical College of Philadelphia, 1909; died June 15, aged 67, of coronary occlusion.

Elmer Ellsworth Mace ● New Palestine, Ind.; Medical College of Indiana, Indianapolis, 1902; served during World War I; died in St. Vincent's Hospital, Indianapolis, July 1, aged 71, of coronary occlusion.

Donald MacIntyre, Big Rapids, Mich.; Michigan College of Medicine and Surgery, Detroit, 1897; member of the American Medical Association; for many years county coroner; past president and secretary of the Mecosta County Medical Society; on the staff of Community Hospital; died June 30, aged 75, of arteriosclerosis.

Robert Donald MacKinnon ● Philadelphia; Temple University School of Medicine, Philadelphia, 1913; instructor in surgery at his alma mater; served in the Boer War and with the Canadian Army Medical Corps during World War I; affiliated with the Temple University Hospital, where he died June 11, aged 70 of arteriosclerosis and abdominal aortic aneurysm.

Marcus J. Magruder, New Orleans; Medical Department of Tulane University of Louisiana, New Orleans, 1889; past president, Orleans Parish Medical Society; and vice president of the Louisiana State Medical Society; affiliated with the Touro Infirmary; in 1946 resigned from the board of administrators of the Tulane Education Fund; received the honorary degree of doctor of laws from Tulane in 1946; died July 4, aged 82, of arteriosclerosis.

Joseph Crockett Manning, Savannah, Mo.; University Medical College of Kansas City, 1913; president of the school board; affiliated with St. Francis Hospital, Maryville, St. Joseph's Hospital and the Missouri Methodist Hospital, where he died June 10, aged 61, of cerebral hemorrhage.

Charles Beverly Martin, Bowling Green, Ky.; University of Louisville (Ky.) Medical Department, 1890; shot to death June 30, aged 83.

Clarence Randle McDonald, Mannford, Okla.; University of Tennessee Medical Department, Nashville, 1909; past president of the Creek County Medical Society; served during World War I; died in the Hillcrest Hospital, Tulsa, June 5, aged 65, of coronary thrombosis.

Neill Smith McLeod, Highland Park, N. J.; Johns Hopkins University School of Medicine, Baltimore, 1924; member of the American Medical Association; died June 7, aged 50.

Thomas Reid McNab, Beverly Hills, Calif.; Medical Department of the University of California, San Francisco, 1903; served during World War I; formerly on the faculty of his alma mater; member of the founders group of the American Board of Surgery; member of the Pacific Coast Surgical Association; fellow of the American College of Surgeons; served on the staff of the Hospital of the Good Samaritan in Los Angeles; died in Honolulu, Hawaii, June 21, aged 70, of acute coronary thrombosis.

James Mansfield Meason, Chandler, Ariz.; Maryland Medical College, Baltimore, 1905; at one time in the Indian Service; formerly mayor of Chandler; county health officer; died in the Good Samaritan Hospital, Phoenix, June 22, aged 70.

Ray Sixtus Nelson ● New York; Syracuse University College of Medicine, 1911; formerly on the faculty of the New York Post-Graduate Medical School and Hospital, Columbia University, New York; served during World War I; on the staffs of Gotham and St. Francis hospitals; died June 18, aged 63, of coronary thrombosis.

William Clark Newcome, Indiana, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1892; member of the American Medical Association; a member of the staff of Adrian Hospital in Punxsutawney; died in Miami, Fla., May 30, aged 80, of cerebral hemorrhage.

Z. Oliver Nobert, Rome, N. Y.; Bennett Medical College, Chicago, 1891; died June 27, aged 86, of carcinoma of the pharynx and coronary sclerosis.

Anthony E. Otto, Alexandria, Ind.; Medical College of Ohio, Cincinnati, 1883; member of the American Medical Association; died June 3, aged 86, of cardiovascular-renal disease.

Wilfred Rossner Parsons, Little Rock, Ark.; University of Arkansas School of Medicine, Little Rock, 1932; member of the American Medical Association; assistant professor of pediatrics at his alma mater; served during World War II; affiliated with St. Vincent Infirmary, Baptist State Hospital, Arkansas Children's Home and Hospital and University Hospital; died June 13, aged 43, of coronary occlusion.

Marion Lee Peoples, Scotia, S. C.; University of Louisville (Ky.) Medical Department, 1891; member of the American Medical Association; died June 16, aged 77.

Wallace Bernard Pyle ● Jersey City, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1897; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; member of the staffs of the Bayonne (N. J.) Hospital and Dispensary, St. Francis Hospital, Jersey City Medical Center and Christ Hospital; one of the founders and a trustee of Fairmount Hospital; died in Orange June 10, aged 71, of cerebral hemorrhage.

Rufus Livius Raiford ● Franklin, Va.; University College of Medicine, Richmond, 1906; founder and until recently chairman of the board of Raiford Memorial Hospital; for many years secretary of the Southside Medical Association; died June 25, aged 67, of coronary thrombosis.

Carl Frost Raver, Charleston, W. Va.; University of Michigan Homeopathic Medical School, Ann Arbor, 1901; served as health officer of Mankato, Minn., Aberdeen, S. D., and La Salle, Ill.; formerly director of the division of vital statistics, state board of health; died June 11, aged 69, of carcinoma of the larynx.

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Simon Warren Reichard, Dayton, Ohio; Medico-Chirurgical College of Philadelphia, 1901; member of the American Medical Association; served during World War I; on the staffs of Good Samaritan and St. Elizabeth's hospitals; affiliated with the Veteran Administration Hospital where he died June 19, aged 70, of cerebral hemorrhage and hypertension.

Anna Magilowa Reinstein, Cheektowaga, N. Y.; Universität Bern Medizinische Fakultat, Switzerland, 1891; died June 21, aged 82, of diabetes mellitus and gangrene of the foot.

Joseph Anthony Rucker, Bedford, Va.; University of Louisville (Ky.) Medical Department, 1893; member of the American Medical Association; past president of the Bedford County Medical Society; for many years secretary of the county board of health; in 1947 was awarded the diamond insignia, symbol of fifty or more years of service with the Norfolk and Western Railway; died June 29, aged 77, of cerebral hemorrhage.

Ralph M. Ryan, Antonito, Colo.; Bennett Medical College, Chicago, 1912; member of the American Medical Association; served during World War I; died in St. Joseph's Hospital, Del Norte, June 30, aged 75, of heart disease.

Edward Saylor, Phillipsburg, Mo.; Missouri Medical College, St. Louis, 1884; member of the American Medical Association; died in St. John's Hospital, Springfield, June 23, aged 93, of fracture of the neck of the right femur and prostatic hypertrophy.

Joseph Scattergood Jr., West Chester, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1929; member of the House of Delegates of the American Medical Association from 1942 to 1944; secretary treasurer of the Chester County Medical Society; medical director of Darlington Sanatorium and Chester County Hospital, where he died June 4, aged 43, of uremia.

Howard Francis Schell, Cincinnati; University of Michigan Homeopathic Medical School, Ann Arbor, 1904; died in the Christ Hospital June 16, aged 68, of uremia and prostatic hypertrophy.

Bernard Schwartz, Philadelphia; Jefferson Medical College of Philadelphia, 1908; member of the American Medical Association; served on the staff of Northern Liberties Hospital, where he died June 25, aged 71, of pulmonary hemorrhage.

Alfred N. Shotwell, Mount Clemens, Mich.; Detroit Medical College, 1884; died in June, aged 90, of cerebral hemorrhage.

John A. Shower, York, Pa.; Southern Homeopathic Medical College, Baltimore, 1894; member of the American Medical Association; died June 24, aged 88, of carcinoma of the descending colon.

Albert Ernest Small ● Melrose, Mass.; Harvard Medical School, Boston, 1900; served during World War I; on the staff of Melrose Hospital; chairman of the board of health; died in Palmer Memorial Hospital, Boston, June 9, aged 72, of recurrent carcinoma of the rectum.

Marianna Eddy Smalley ● Ann Arbor, Mich.; University of Michigan Medical School, Ann Arbor, 1931; instructor in internal medicine at her alma mater; member of the American Trudeau Society, American Association of the History of Medicine and the Michigan Trudeau Society; on the staff of St. Joseph's Hospital; died June 21, aged 44.

Francis Henney Smith ● Abingdon, Va.; University College of Medicine, Richmond, 1904; specialist certified by the American Board of Internal Medicine; past president of the Southwestern Virginia Medical Society and the Medical Society of Virginia; served during World War I; a member of the state board of medical examiners; fellow of the American College of Physicians; affiliated with the George Ben Johnston Memorial Hospital; died July 1, aged 67.

Horace R. Stauffer, Nappanee, Ind.; Rush Medical College, Chicago, 1883; for many years member of the state legislature; died July 2, aged 90.

Dudley Donnelly Stetson ● Santa Fe, N. M.; Colorado School of Medicine, Boulder, 1905; specialist certified by the American Board of Dermatology and Syphilology; formerly on the faculty of the New York Post-Graduate Medical School and Hospital, Columbia University; at one time on the staffs of Lincoln and Roosevelt hospitals in New York; died June 14, aged 70, of heart disease.

John Coleman Stiles, Dallas, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1898; member of the American Medical Association; died in the Methodist Hospital May 11, aged 74, of cerebral hemorrhage and pyelonephritis.

Charles Frederick Stotz ● Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1898; fellow of the American College of Surgeons; a trustee of the Chicago Medical Society; a member of the "Fifty Year Club" of the Illinois State Medical Society; connected with Walther Memorial Hospital since its founding, serving as chief of staff, president of staff and president emeritus; died July 18, aged 75, of carcinoma.

Frank Raphael Strong, Brewerton, N. Y.; Syracuse University College of Medicine, 1904; died in the University Hospital, Syracuse, June 20, aged 72, of a hip fracture received in a fall and arteriosclerotic heart disease.

William Herman Sugarman ● Brooklyn; Cornell University Medical College, New York, 1914; specialist certified by the American Board of Internal Medicine; affiliated with the Brooklyn Hebrew Home and Hospital for Aged and the Jewish Hospital, where he died June 23, aged 59, of acute coronary occlusion with myocardial infarction.

Frank Augustus St. Sure, Haiku, Hawaii; College of Physicians and Surgeons of San Francisco, 1900; veteran of the Spanish-American War; member of the American Medical Association; died June 22, aged 74.

Carol Lincoln Sweet, Los Gatos, Calif.; University of the City of New York Medical Department, New York, 1882; formerly president of the Idaho State Medical Association and secretary of the Idaho State Board of Medical Examiners; veteran of the Spanish-American War and surgeon general of the Idaho National Guard; died June 19, aged 88, of senility.

Franz J. Swoboda, Omaha; University of Nebraska College of Medicine, Omaha, 1905; died June 18, aged 68, of cerebral thrombosis.

Samuel L. Thorpe ● Major, U. S. Army, retired, Seattle; Northwestern University Medical School, Chicago, 1893; entered the medical corps of the U. S. Army as a captain in 1920; retired Sept. 30, 1933 for disability in line of duty; served during World War I; died in Madigan General Hospital, June 4, aged 78.

William A. Tisdale, Seminary, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1890; died in the Methodist Hospital, Hattiesburg, June 7, aged 85.

George Henry Torney ● Brookline, Mass.; University of Pennsylvania Department of Medicine, Philadelphia, 1894; member of the American Psychiatric Association and the New England Society of Psychiatry; medical director, superintendent and owner of the Bournewood Hospital; died June 1, aged 75, of dissecting aneurysm of the aorta.

Camillo Eugene Volini ● Chicago; Loyola University School of Medicine, Chicago, 1933; served as president of the Chicago Tuberculosis Society; resigned in January 1948 as superintendent of clinics for the Municipal Tuberculosis Sanitarium, where he had been on the staff for many years; died in Columbus Hospital June 22, aged 40.

Joseph Francis Walsh ● Eureka, Calif.; Cooper Medical College, San Francisco; 1909; died May 28, aged 63, of heart disease.

Max Wershow, Los Angeles; University of Michigan Medical School, Ann Arbor, 1920; died June 17, aged 60.

Euclid Clarence Wills, Phoenix, Ariz.; Medical College of Virginia, Richmond, 1906; died June 6, aged 63, of coronary disease.

Chester Anderson Witmer ● Waycross, Ga.; University of Virginia Department of Medicine, Charlottesville, 1911; served in the medical corps of the U. S. Army during World War I; past president of the Ware County Medical Society and the Eighth District Medical Society; city physician; fellow of the American College of Surgeons; chief of staff, Ware County Hospital; local surgeon for the Atlantic Coast Line Railroad; died May 7, aged 60, of mesenteric thrombosis.

Jesse Charles Woodward ● Payette, Idaho; Gross Medical College, Denver, 1900; died June 23, aged 75, of coronary occlusion.

DIED WHILE IN MILITARY SERVICE

Robert Oscar May, Pittsburgh; Temple University School of Medicine, Philadelphia, 1945; interned at St. Francis Hospital; began active duty as a lieutenant (jg) in the medical corps of the Naval Reserve in April 1946; died in Italy Sept. 26, 1947, aged 27, of injuries received in an automobile accident.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Sept. 4, 1948.

Private Practice and the National Health Service

The National Health Service is designed to make the practice of medicine entirely socialistic; however, it has come into force with remarkably little friction. Some trouble has arisen in connection with what are called "health centers." These promise to be a useful innovation by providing buildings where physicians can cooperate and where their time will be saved by a clerical staff undertaking routine duties. The Minister of Health has refused the request of physicians that they should be allowed to treat their private patients at these centers. The general purposes committee of the Birmingham National Health Executive Council is so seriously concerned with this refusal that it proposes to take energetic measures to get the ruling reversed at the first annual meeting of the Executive Councils' Association in London. The objection is made that if the Minister's decision is adhered to it may be impracticable to operate health centers. If physicians are not allowed to treat private patients at health centers they will be forced to maintain at extra expense separate offices and to attend at them. Different offices for private and public patients might cause public patients to regard health centers as charitable institutions. Some physicians have intimated that if the Minister's decision is adhered to most general practitioners will not participate in the health center schemes. This refusal of the Minister is only one symptom of the socialistic Government's antagonism to private practice. There seems little doubt that they would have liked to abolish it and convert the doctors into civil servants. Only the stand made by the profession against payment by salary compelled the Government to accept payment by capitation. It was realized by the profession that payment by salary would only be a step to the reduction of physicians to officials entirely controlled by the state. But this remains a danger of the future, which will probably materialize if socialism remains dominant.

The Government's antagonism to private practice is illustrated by another incident. Those who prefer to remain private patients of physicians can continue to do so, but they will be taxed for the National Health Service exactly as those who use it. The modest request was made on their behalf that, as they had foregone the free doctoring, they might be allowed to obtain the free medicine given to those who use the Service, but the Minister has again refused.

Cost of Dentistry Under the National Health Service

The dentists have more strongly opposed the scheme of the National Health Service than the physicians. In a press interview Mr. Buchanan, secretary of the British Dental Association, states that 30,000 estimates for dental work are being received every day by the Dental Estimates Board and that the average cost is more than $20. This means that the scheme is now costing more than $600,000 a day, while the Government estimate for a full year is only $28,000,000. This means that the scheme is costing more than seven times the Government estimate. Many dentists have a large income, but the present scheme must break down sooner or later, and the Ministry of Health will be driven to a reconsideration of the whole matter. The secretary claims that this result shows the wisdom of the policy of grant-in-aid advocated by the association but rejected by the Ministry of Health. The association is also demanding full clinical freedom and a guarantee that the Minister will not introduce a full time dental service by regulation. At a meeting of the Council of the Association it has been decided to send a further letter to every member advising him not to enter the National Health Service.

This staggering increase of cost of the dental service is, of course, due to the offer of "something for nothing" which characterizes socialistic schemes. Every one who can possibly do so wants to share in the spoils. It might be rejoined that the service is really not free, as the beneficiaries pay by their weekly contributions, but their payments amount to only part of the cost, the rest being made up by the state. In any case the motive to share in the distribution remains exactly as if no contributions were made. This increased cost holds for all the industries that have been socialized. The cost of coal is more than doubled, and notwithstanding this, a loss has been made in the working of the industry. In state-owned industries no one has any interest in economy or efficiency. Late in the day some of the more intelligent members of the Labor Government have grasped the elementary economic truth that a good output is essential for the prosperity of the country and have appealed to the workers to give this. But the politicians have had to admit that the response was "disappointing." Why should it be otherwise when the men are in no danger of dismissal, as in the case of private enterprise. Altruism is no part of the trade union propaganda on which they are fed.

Returning to the dentists, the Ministry of Health says that 7,000 have joined the service, but the association states that almost the whole of this number can be accounted for by dentists who are not members of the association.

PARIS

(From Our Regular Correspondent)

Aug. 15, 1948.

Research on the Antigens of Koch's Bacillus

Miss Choucroun has made a communication to the National Academy of Medicine on two isolated fractions of Koch's bacillus, one being protein and the other lipopolysaccharide. She obtained them from an oily extract of dead tubercle bacilli precipitated by the addition of dioxane. The mixture of those two substances dissolves in chloroform to which is added 5 per cent methanol, and their separation is effected by petroleum ether. The author has noted that the lipopolysaccharide fraction plays an important part in the development of hypersensitivity to tuberculin. The purified protein fraction injected into guinea pigs has no sensitizing power, but 20 micrograms of lipopolysaccharide added to 100 micrograms of the proteinic substance is sufficient to give it a sensitizing capacity. Boissevain and Schaffer have brought to light the relation between the acid reistance of Koch's bacillus and its sensitizing capacity; rendered non-acid-resisting by acid hydrolysis, it loses at the same time its sensitizing power. Miss Choucroun has proved that the liposaccharide is the factor responsible for this acid resistance. She found in the products of hydrolysis of acid-resisting bacilli the products of hydrolysis of lipopolysaccharide, mycholic acid and sugars, and, moreover, she has been able to give non-acid-resisting "skeletons" capacity of acid resistance by adding to them the whole lipopolysaccharide, or the mycholic acid and its sugar. The lipopolysaccharide fraction is also the only antigenic complex; i. e., the only one capable of determining the formation of polysaccharide antibodies. The author suggests that those polysaccharide antibodies play an important part in the mechanism of acquired resistance.

Treatment of Eczema

The first works on the treatment of infantile eczema by unsaturated fatty acids (reported to the Medical Society of the Paris Hospitals) have just been published in France. E. Azerad and Crupper have treated 30 children with satisfactory results. They emphasize the remarkable eutrophic effect of this diet. The percentage of linoleic acid in lard varying according to

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various factors, the authors have chosen to substitute for lard purified preparations of linoleic acid, or even of an ester of this acid easier to administrate and the action of which appears more rapid. J. Charpy (Dijon) has presented his results of three years of experiments in 1,200 cases. The author obtained conclusive results in 80 per cent of cases of various forms of this disease. He gives doses of 20 to 100 Gm. of lard per day according to age and weight. The simultaneous administration of certain elements of the B complex, especially vitamin B_6 in the dose of 0.10 to 1 or 2 Gm. per day has a synergic effect, permitting at the same time the reduction of the dose of unsaturated fatty acids. For the treatment of certain true or allergic eczemas in the infant, the author studied replacing vitamin B_6 with vitamin B_5. J. Champougny and E. Le Breton have recently proved that vitamins B_6, B_5 and B_3 are coenzymes of the "desaturase" of superior fatty acids, but this process occurs only after a previous phosphorylation. The author is studying the way of insuring the maximum of this phosphorylation in the organism, through which he expects an increase of the therapeutic effect. With unsaturated fatty acids and vitamin B_6 the author associated oral intestinal vaccines which seem to increase the effectiveness of the two essential elements of this therapy. He limits the local treatment to dressing with lard or with a mixture of vitamin B_6, wool fat and lard. He insists on the necessity of eliminating allergens, which may, by external contact or by internal route, produce the cutaneous unbalance.

New Treatment of Arteritis of the Limbs

With a view to measuring the blood circulation of limbs in arteritis, Lemaire, Loeper and Housset injected oxygen into the arterial trunk; they noted improvement in most of the patients. They have just reported to the National Academy of Medicine their study of 15 patients: 5 with diabetic arteritis, 7 with senile arteritis, 2 with specific arteritis and 1 with acute arteritis. The injections were made in the femoral artery at the crural arcade. They at first used gaseous oxygen in a volume of 70 to 200 cc. injected in one to two minutes. Recently, in order to facilitate the injection, the authors used 2 cc. of hydrogen peroxide at 30 volumes mixed with 3 cc. of isotonic sodium chloride solution, which yields roughly 90 cc. gaseous oxygen. The results of this treatment, lasting from one to three weeks, are striking: disappearance of the pain and cramp in the calves when walking and in the decubitus position. The effectiveness of this therapy is much more lasting than that of the classic vasodilators. During the injection, the patient experiences sensations of tingling and of burning in the foot and calf, followed either by pallor of the limb or by disks of erythrosis on the leg, scrotum and even the abdomen; the same phenomena, but less accentuated, occur sometimes on the limb which has not received an injection. A few hours afterward the patient has a sensation of heat which persists. Immediately after the injection or later the oscillometric index is not modified; the cutaneous temperature falls for fifteen to thirty minutes and then rises again, and surpasses the previous rate by 2 to 3 C. Failures are rare. Reactions, varying from one patient to another, may occur in the form of lumbago, imperative desire to urinate, violent colic with emission of several stools, slight shivering, temperature of 38 C. (100.4 F.) and slight but temporary fall of the arterial pressure. Only one fatal accident has occurred, in a 55 year old diabetic patient with arteritis of the superior and inferior limbs, who after an efficacious injection, without incident, in the leg was while seated given another one in the subclavian artery. A few seconds, after the beginning of the injection a tonic crisis occurred, then a hemiplegic coma and death a few hours afterward. The authors emphasize that such accidents would never occur if the precaution is taken to put the patient in the Trendelenburg position. Provoked gaseous emboli in the arteries of the limbs are without any danger whatever, oxygen combining rapidly with hemoglobin. The authors think that the therapeutic effect of this method is due either to compensation for the loss of oxygen due to the slowing of circulation in the arterioles or to reactivation of cellular cytochromes. Moreover, they say such gaseous emboli provoke an arteriolocapillary vasodilation.

OSLO

(From Our Regular Correspondent)

Sept. 8, 1948.

Don't Just Listen! Take Notes!

Early every September, Oslo suddenly turns academic and university conscious. Everywhere one sees students' caps, with their heavy black silk tassels, crowning thousands of heads, some gray or bald. This emblem of the freemasonry among the intellectuals from all parts of Norway culminates in the University Hall, where this year, on September 2, Professor Otto Lous Mohr, rector of the university, delivered an address. He pointed out that in the early days of the university 60 per cent of the entrants came from the professional classes. Now only 14 per cent do so. Now an academic career is open to all with brains, and 9 per cent come from the homes of farmers and fishermen. Every fifth student is now a woman. Professor Mohr referred with grateful appreciation to the help given to the university by various American organizations, including the Rockefeller Foundation, which has provided not only fellowships and travel grants, but also funds for the purchase of scientific publications. Professor Mohr awarded the much coveted prizes of the year, including the Monrad-Krohn prize for neurologic research, won this year by Dr. Sigvald Refsum for his work on heredopathia atactica polyneuritiformis.

In his first lecture of the autumn term, on Saturday, Sept. 4, Professor Olav Hanssen welcomed the occupants of crowded benches to the study of medicine. Then he sparkled for a solid hour. Behind the sparkle and the whimsical anecdotes was much shrewd advice such as: "Don't just sit there and listen! Take notes all the time!" Then he demonstrated a patient who had been knocked down by a cyclist and had obscure signs and symptoms referred to one leg. Examined successively by a physician, a surgeon and a psychiatrist, he had been suspected of a compensation-hungry neurosis. What a pity that neither the physician nor the surgeon nor the psychiatrist had consented to the roentgenologic examination for which the patient had pleaded! For when at last a roentgenogram was taken, it showed a fracture of the fibula. If only we could learn to take notes of all we hear and see, and take roentgenograms whenever we are in doubt!

Professor Kristine Bonnevie

Miss Kristine Bonnevie, the first woman to gain the title of professor at the University of Oslo, has just passed away, much loved and greatly honored. She was born in Oslo in 1872, and it was here that she passed most of her life, although she was of international stature and had worked in Germany, Switzerland and the United States. She took her degree of Doctor of Philosophy in 1906 and was appointed professor of zoology in 1912. Her scientific interests covered a wide field, and she made important contributions to embryology and the problems of heredity. As recently as last summer, at the age of 76, she took part in the International Congress on Heredity in Stockholm, then as always rubbing shoulders with fellow scientists from all over the world with that unassuming ease which made her such an attractive fellow traveler in life.

To the younger generation and in wide circles, Professor Bonnevie was the beloved "Tante Kristine" to whom one came with one's troubles, whether they were personal or scientific.

Though she never married, she was the most motherly of souls, always on the lookout for an opportunity to give a helping hand when one was in difficulties. During World War I she organized in a cellar in one of the university buildings a kitchen restaurant in which students were provided with meals at cost price. During World War II, though no longer holding the chair of zoology, she again fed young students with unobtrusive efficiency. They showed their appreciation by electing her to places of honor in their various associations, and she was for some years the chairman of the women students' choir. But she was, perhaps, at her best when at work at the biologic station in the Oslo fjord, clad as a seaman, sou'wester and all, reveling in the riches dredged up from the bottom of the sea, and sharing them with her students with open-handed generosity.

Sven Oftedal

He was still rather young when he died, but his career was so brilliant and his personality so charming and forceful that he has left an indelible impression. He was born in Stavanger in 1905 into a family already noted for intellectual gifts. After qualifying as a doctor in 1930 he served as an intern successively in a general hospital, a private asylum and a Red Cross sanatorium. Then, in 1933, he settled down in his native town as a general practitioner. His success in this field did not prevent his taking an active interest in local government, and from 1933 onward he took a prominent part in social work in Stavanger. When the Germans invaded Norway, his glowing patriotism qualified him for arrest as a hostage for his town. A little later the Germans removed this troublesome patriot to the concentration camp at Grini, where, as everywhere else, he soon became a leader of his fellow beings. A pestilential fellow from the German point of view, he had yet to be employed in key positions at Grini. Set free after some time on probation, he became such a nuisance and even danger to the Germans that he had to be arrested again, and, after they had tried to keep him quiet in various prisons in Norway, they sent him in 1943 to the notorious concentration camp of Sachsenhausen in Germany. Here he remained until the end of the war, always the acknowledged leader of his fellow sufferers. On Oftedal's return to Norway in 1945, his appointment to high office was a foregone conclusion. As a member of the Government and head of the Department for Social Affairs, he took an active part during the next three years in the social legislation which has had such far reaching effects in the postwar period. He was still in office and had been on sick leave for only a few weeks when an infarct of the heart ended his career.

SPAIN

(From Our Regular Correspondent)

Aug. 12, 1948.

National Institute of Medical Science

The National Institute of Medical Science was founded as a dependency of the Higher Council for Scientific Research by Decree of Dec. 16, 1942, with the object of coordinating the work of all state research centers and more especially of the faculties of medicine in Spanish universities. During its five years of existence and development, the number of its departments has progressively increased, as well as the amount of work done. Twenty-one departments are functioning at present, dealing with the following disciplines and specialties: morphology, human and comparative physiology, immunology and microbiology, experimental pharmacology, metabolic pathology, digestive pathology, internal medicine, experimental surgery, legal medicine and toxicology, medical biochemistry and history of medicine. As a general rule, these departments are linked up with the university departments or with other recognized teaching centers outside the university, such as the Postgraduate Institute at Valdecilla (Santander) and the Basurto Hospital at Bilbao. The institute publishes a quarterly volume comprising papers on research and called *Trabajos del Instituto de Ciencias Medicas*, of which ten or eleven issues have already appeared, full of important original papers.

The institute looks after the training and guidance of young medical research workers and sends many of them to research centers abroad to acquire knowledge and practice of basic technics and principles on which to found their future work in Spain. In this respect, the institute fills the place of the old Studies Extension Board.

The head of the institute is the dean of the Madrid Faculty of Medicine, Professor F. Enriquez de Salamanca, who has been doing research since 1925 on the examination and physiology of the human stomach on the same lines as the work started by Lewin and the Katsch school somewhat later, in 1927.

He has been able to determine the volume of secretion and has succeeded in measuring for the first time the rate of secretion in the course of digestion. He has ascertained the variability of the concentration of gastric juice, which may go from 0.5 Gm. per thousand of chloride to more than 6 Gm. per thousand. He has observed a parallelism between the rate of secretion and chloride concentration, but as between different days in the same subject and as between various subjects compared with one another, he found that the quantity of juice was in inverse ratio to the concentration and, in all of them, at the end of digestion there was an even more abundant secretion, though this was poor in chloride and acid.

GERMANY

(From Our Regular Correspondent)

Aug. 31, 1948.

Postwar Goiter in Germany

After the first world war, German physicians described an increased incidence of goiter, even in parts of the country normally free from goiter, like Nuremberg, the Ruhr district and the Northern German plain. In 1924, there was still a high percentage of patients with goiter among adolescents. It decreased markedly toward the end of the twenties.

The same trend has been noted during and after the second world war. This time, however, the situation is complicated by the influx of evacuees and refugees into these districts from parts of former Germany where goiter has always been endemic, and also by the fact that a large proportion of German youths were evacuated from cities and sent to different parts of the country during the war, some of which are also goiter districts. However, various authors writing on the subject have stressed that the appearance of endemic goiter is by no means restricted to such cases. Comparisons of groups of children of early school age showed a moderate increase of the size of the thyroid gland in less than 1 per cent in the late twenties, against more than 20 per cent recently. The same case rate is found in children 11 to 12 years of age. If old and new residents of Central Germany are counted separately, the figures show that among the static group about one fifth and among the refugee group about one third of the children have enlarged thyroid glands.

The cause of this situation is not well understood. There seems to be a lower incidence of goiter in the socially higher strata; therefore, lack of proteins has been considered to be an etiologic factor. Treatment with iodine is of doubtful value. It has been said that these postwar goiters in adolescents are often connected with a delayed sexual development. This would point to an advisability of polyhormonal treatment.

Infantile Paralysis in Bavaria

A serious outbreak of poliomyelitis has occurred in all of Bavaria, particularly in the towns of Hof, Regensburg and Straubing. Health authorities caution that the peak may not be reached before the end of this month. Within one week, the number of affected persons rose from 250 to 410. Eighteen deaths were reported.

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Correspondence

MEDICAL EDUCATION IN CHILE

To the Editor:—During the month of July of this year I had the opportunity of visiting most of the important hospitals and medical institutions in Santiago de Chile. It was possible during this time to analyze the organization of their medical services. I was greatly impressed with the very high plane of teaching of medicine in the University of Chile.

Internal medicine is taught on four major services, each headed by a professor of medicine. Two of these services are in the Hospital del Salvador. I particularly wish to comment on the high character of medical teaching on the services of Drs. Hernan Allesandri and Armas Cruz of that hospital because I had the opportunity of observing the work on these two services closely. I have no reason to feel that the medical services of Dr. Garreton at the Hospital San Borja and of Dr. Prado Tagle at the Hospital San Vicente are in any way inferior to the services at the Hospital del Salvador, with which I am more familiar.

On both these services at the Hospital del Salvador, Drs. Allesandri and Armas Cruz have associated themselves with a group of young physicians well trained in the subspecialties of internal medicine. Many of these young men have been trained in the United States. On these two services, gastroenterology, in which I was particularly interested, was integrated into the medical services and supervised by several well trained young gastroenterologic internists. These two departments of gastroenterology were as well organized as any that I have seen in this country. All the teaching devices utilized in gastroenterology were on hand, and they were applied by well trained men. I was impressed by the close integration of all divisions in medicine under the leadership of these two excellent physicians. Research projects were actively going on in many of the subdivisions of medicine, and the close integration of the various subspecialties afforded an ideal setup for the carrying out of important clinical research projects.

The criticism often made of Latin American medicine concerning the continuation of older European methods of practice and teaching certainly does not apply to the teaching of internal medicine in the University of Chile in Santiago. The chiefs of the medical services are well versed in modern American medicine, and in some respects their organization is better than that on some of our medical services in this country. For example, all deceased patients are subjected to autopsy by a well trained pathologist assigned to each of these medical services. Each week the students working on both services have the opportunity of attending a medical pathologic conference in which all cases are completely reviewed and discussed. The clinical, roentgenologic and laboratory features of each case are presented and discussed before the necropsy findings are given. Because of the universal autopsy system and the full time services of a pathologist on each medical service, this material can be ideally integrated and important clinical pathologic studies in many diseases are made possible. For example, the analysis of a tremendous number of cases of hepatic cirrhosis, which is common in Chile, is now being prepared on the service of Dr. Armas Cruz and important papers dealing with a large experience with infectious hepatitis are being prepared by Drs. Allesandri and Ducci.

Finally, I should like to comment on the fine scientific spirit and on the medical camaraderie, which are so obvious to the visitor in Santiago. These Chilenos are practicing *factual* medicine on a high plane, and a closer association with our colleagues in Chile is highly desirable. Important contributions in medicine may be anticipated from this newly developed medical center.

Before closing I should like to pay my respects to Dr. Gandi, the representative of the Institute of Inter-American Affairs in Chile. This gentleman, ideally suited by personality and training to the position which he holds, has contributed greatly to the healthy spirit of collaboration between the medical scientists of Chile and those of the United States.

H. L. Bockus, M.D., Philadelphia.

EFFECT OF PROCAINE ON THE HEART

To the Editor:—The hazards attending the intravenous administration of procaine, recently advocated in the treatment of bronchial asthma and other conditions, have been pointed out by Waldbott in THE JOURNAL, April 26, 1947, and again in Queries and Minor Notes in the Aug. 21, 1948 issue.

The hazards of this procedure are further indicated by our recent experimental electrocardiographic observations in the dog (*Am. Heart Journal*, in press). These studies revealed that intravenously administered procaine is capable of exerting a direct effect on the heart. The most striking result was a powerful depressant action on the conduction system, manifested by a tendency to prolongation of the P-R and QRS intervals, and leading to the development of auriculoventricular and intraventricular block. Other findings suggested some alteration in the invasion and retreat patterns of impulse spread, indicating an effect on the myocardium per se. The deleterious effects of the drug on the heart appeared to bear a close relation to the rapidity of the injection and the quantity employed; in 1 of our animals rapid intravenous administration of a relatively large dose induced a state of "chaotic heart action" with multiple ectopic pacemakers. These investigations were on experimental animals. While dosage-toxicity correlations, with respect to cardiac effects, have not been made in man, it is likely that a pharmacologic parallelism exists. The intravenous injection of procaine consequently should be undertaken with additional caution in persons with inflammatory or "degenerative" cardiac lesions.

Morris Wilburne, M.D.
Milton H. Uhley, M.D.
Beverly Hills, Calif.

PENICILLIN AND MALARIA

To the Editor:—I was interested to read in the Aug. 28, 1948 issue of THE JOURNAL an abstract from the *Indian Medical Gazette* (82:511-558 [Sept.] 1947) of an article by Deshmukh which states that penicillin seems to have a synergistic action in the treatment of acute attacks of malaria and that "penicillin controls the pre-erythrocytic stage of the malarial parasite." There is not a shred of evidence that I know of, unless one accepts the conclusions of Deshmukh, that penicillin has any effect on malaria in man. On the contrary, there is evidence that penicillin has no effect.

During the war years I had an opportunity, during studies of new antimalarials, to observe for long periods of time a great many patients with relapsing vivax malaria. Many of them were given penicillin for surgical or medical conditions other than malaria, and many suffered malarial relapses during and after administration of penicillin. So much for the pre-erythrocytic stage.

During the past year I have participated in a study of a method of inducing malaria with parasitized blood preserved by freezing. In approximately 20 cases of neurosyphilis with induced malaria penicillin was given during the incubation period and the course of the malarial attack. There was no apparent effect of the penicillin on the development or subsequent course of malaria.

George M. Saunders, M.D., St. Louis.

Medical Economics

SCOTTISH EXPERIMENTS IN SOCIAL MEDICINE

A Review by Frank G. Dickinson, Ph.D., Director, Bureau of Medical Economic Research

The Department of Health for Scotland, under the direction of Sir Andrew Davidson, has undertaken several studies and experiments.[1] Analysis of morbidity statistics for the immediate prewar period revealed a surprising amount of chronic incapacity among the working population, particularly at ages under 40 years. Of 25,900,000 working days lost by 1,800,000 insured wage earners in the year ending June 30, 1948, 44 per cent was due to illnesses rendering 31,000 persons unfit for work throughout the entire year. Clinical data were obtained for over 50,000 patients incapacitated for three months or longer; 1,000 of these cases were subjected to intensive study. Results indicated the importance of early diagnosis and treatment in conserving the working capacity of wage earners; they also showed a need for periodic review of diagnosis and treatment in prolonged illnesses, with close cooperation between personal physician and specialist services.

AN EXPERIMENT IN PREVENTIVE MEDICINE

Early in 1942, the department instituted a program to prevent chronic invalidism by minimizing breakdown in the health of war workers. Within one and one-half years some 5,000 workers were given special clinical examination and admitted to war emergency base hospitals for detailed investigation or to country mansions for intensive convalescence. Most of these patients showed vague ill health, some degree of debility and often anxiety states due to overwork. Their response to treatment indicated the value of rest and recreation in combating fatigue which might otherwise lead to prolonged physical and mental illness.

AN EXPERIMENT IN REHABILITATION

In January 1943, the department instituted a scheme to return the sick and injured to active employment. A fitness center for disabled miners was opened; other workers were later admitted. The program consisted of activity by the patient under the direction of a physician. Average length of stay in the center is from fifty to eighty days; the discharged patient is checked by follow-ups after two and six months. Results up to June 1947 show that of 1,900 miners treated, 63 per cent were able to continue their former work, 19 per cent were fit for light work, 5 per cent were fit for alternative employment and only 1 per cent were unfit at the end of the course. Of 270 other workers treated, 69 per cent returned to their former work and less than 1 per cent remained unfit for employment. Rehabilitation methods cannot cover deficiencies in surgical or medical treatment, and must be varied with the needs of the patient. Moreover, the study indicates the rehabilitative value of returning the patient to work for which he is fit as soon as possible.

MEDICAL CARE IN A LARGE RURAL AREA

In 1912, a committee of the British Parliament made a study of medical care in the Highlands and Islands, an area including almost half of the land surface of Scotland, lying to the north and west and inhabited by 300,000 persons. Due to the sparseness and poverty of the population, inadequate transportation and communication, and geographic and climatic difficulties, medical service was uncertain for the people and hazardous for the physician. To remedy this situation, Parliament established the Highlands and Islands Medical Service Fund, under which grants were approved for (1) physicians, (2) nursing services, (3) specialist, hospital and ambulance services and (4) telegraph and telephone services. The scheme endeavors to supply necessary medical services to every person in the area and to assure each practitioner a definite minimum net income. "Scheme patients" unable to pay regular fees and not covered by the National Health Insurance scheme receive medical care on the basis of a schedule of modified fees. To compensate for his reduced earnings, the Highlands and Islands doctor receives a yearly grant from the Medical Service Fund, along with financial aid for housing and facilities for holiday leave and postgraduate courses.

Hospital and specialist services have been developed in the area with the aid of grants from the Medical Service Fund. Ambulance services have been provided to transport patients to and from hospitals. County and district nursing associations have been organized to provide nurses fully qualified in general nursing, obstetrics and domiciliary work. Grants from the fund assure each nurse a reasonable salary, suitable residence, means of transport and telephone service.

The declared aim of the Department of Health for Scotland has been to provide necessary finance and a flexible and friendly central administration. Considerable evidence is cited to attest to the success of the Highlands and Islands Medical Service program. The standard of health in the Highlands and Islands area has risen steadily in the past thirty years. Facilities for medical care are now available to inhabitants in the most remote sections. The department has had no difficulty in obtaining qualified physicians, specialists and nurses to participate in the scheme. The Highlands and Islands practitioners have recently expressed their satisfaction with the administrative handling of the program. Judging by this report, remarkable progress has been made in the provision of medical care in this difficult and extensive rural area of Scotland.

1. Davidson, A.: Scottish Experiments in Social Medicine, Bull. Johns Hopkins Hosp. 82:479-495 (April) 1948.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Application of Res Ipsa Loquitur in Case of Silver Nitrate Burn.—The plaintiff sued for damages alleged to have resulted from the negligence of the defendant physician. From a judgment for the defendant, the plaintiff appealed to the district court of appeal, first district, division 1, California.

The plaintiff testified that, because of a varicose vein condition, she had visited the defendant physician and that he had directed her to enter a hospital. In the hospital the defendant had her stand beside the bed while he outlined on her legs certain veins that were to be surgically removed. The marks were made with a silver nitrate pencil which the nurse had brought to the defendant, and there were four such markings on each leg, two above the knee and two below. Shortly after the markings were put on, the plaintiff's legs began to burn and to become very inflamed around the areas marked by the defendant, and in a short time blisters formed at such areas. The pain was very severe. When the defendant physician arrived for the operation the next morning he examined her legs and told her that the operation would have to be postponed because the burns were too severe. The defendant, called as a witness by the plaintiff, admitted having made the markings on the plaintiff's legs and said that the purpose of such markings was to outline the veins to be removed. When a patient is lying down on the operating table the veins tend to relax and disappear, but when the patient is standing the veins stand out and are easily seen. The defendant said that ordinarily there is no unfavorable reaction from the application of silver nitrate but he admitted that the solution applied to some persons' legs did cause burns and that he did not know ahead of time whether or not the plaintiff was susceptible to such solution, not having made any prior test. He said that he procured the silver nitrate from the stock supply of the hospital, that he did not know who manufactured it and that he had made no attempt to ascertain that fact. He was not aware of the potency of the solution, nor did he attempt to investigate after the patient was burned to ascertain the strength of the solution. The defendant also testified that it was the common practice of doctors in San Francisco to mark off the area to be operated on with a silver nitrate solution and that it was also standard practice to mark off the operating area without first making any tests.

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He stated that prior to his treatment of the plaintiff he had performed three or four hundred such operations and that everything he did in this case was performed according to the ordinary standard of practice of surgeons in San Francisco.

On the basis of this evidence the trial court granted the defendant's motion for nonsuit and pointed out that the burden is on the plaintiff in such a case to show that the doctor did not possess and use the degree of skill possessed by similar practitioners in the same locality. On appeal the plaintiff urged that the doctrine of res ipsa loquitur was applicable to this case. The doctrine of res ipsa loquitur, said the Supreme Court, applies where the accident that occurred was such that in the ordinary course of events, the defendant using ordinary care, it would not have happened and where the instrumentality causing the accident was under the control of the defendant. The first requirement, continued the court, is clearly met in the instant case. Certainly it cannot be contended that the severe burning of patients is the normal result of the preparatory treatment for operation to remove varicose veins. The defendant contended, however, that the doctrine was not applicable in this case because it was not shown that the doctor had exclusive control of the silver nitrate solution, and in this connection the defendant pointed out that the evidence showed that the hospital furnished the silver nitrate pencil to the defendant. The evidence also showed, however, that the nurse asked the doctor if the equipment so furnished was what he desired and the doctor replied that it was.

After citing a number of other cases in which the doctrine of res ipsa loquitur was applied to malpractice proceedings the Supreme Court said that the doctrine did apply in this case and the physician was held liable. The judgment in favor of the defendant was therefore reversed.—*Hurt v. Susnow, 192 P. (2d) 771 (Calif., 1948).*

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Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I & II.* Various Centers, Feb., June, and Sept., 1949. *Part II.* April, 1949. Exec. Sec., Mr. K. S. Elwood, 225 S. 15th St., Philadelphia 2. *Pa. Part III.* Boston & New York, Autumn. Sec., Dr. J. S. Rodman, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 18. *Oral.* Chicago, Oct. 13-15; Philadelphia, Nov. 3-5; San Francisco, date not set. Candidates now eligible for the orals cannot be promised a place in 1949. Sec., Dr. W. A. Werrell, 11 W. Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral,* Chicago, June 1949. Final date for filing application is Jan. 1949. Sec., Dr. W. J. German, 310 Cedar Street, New Haven, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Part I.* Various Centers, Feb. 4, 1949. Final date for filing application is Nov. 1. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh 1.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* St. Louis, Oct. 15-19. Sec., Dr. S. J. Beach, 56 Ivie Rd., Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPEDIC SURGERY: *Part I.* Various Centers, April & May. Final date for filing application is Dec. 31. Sec., Dr. Francis M. McKeever, 1136 W. 6th St., Los Angeles 14.

AMERICAN BOARD OF OTOLARYNGOLOGY: New York, Spring, 1949. Sec., Dr. D. M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Atlantic City, Nov. 17-19. Sec., Dr. Lee F. Hill, 718 Royal Union Bldg., Des Moines, Iowa.

AMERICAN BOARD OF PLASTIC SURGERY: Examinations are given in June and November of each year in the home town of applicants. Sec., Treas., Dr. Louis T. Byars, 400 Metropolitan Bldg., St. Louis, Mo.

AMERICAN BOARD OF SURGERY: *Written.* Various Centers, March 1949. Final date for filing application is Dec. 1. Sec., Dr. J. S. Rodman 225 S. 15th St., Philadelphia.

AMERICAN BOARD OF UROLOGY: Feb. 1950. Sec., Dr. Harry Culver, 7935 Sunnyside Road, Minneapolis 18, Minn.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 28-30, 1949. Sec., Dr. D. G. Gill, 319 Dexter Ave., Montgomery.

ARKANSAS: * Little Rock, Nov. 4-5. Sec., Medical Board of the Arkansas Medical Society, Dr. L. J. Kominsky, Texarkana. *Eclectic Examination.* Little Rock, Nov. 4. Sec., Dr. C. H. Young, 1415 Main St. Little Rock.

CALIFORNIA: *Oral,* Los Angeles, Nov. 20-21. *Written,* Sacramento, Oct. 18-21. Sec., Dr. Frederick N. Scatena, 1020 N Street, Sacramento 14.

CONNECTICUT: * *Examination.* Hartford, Nov. 9-10. Sec., Dr. Creighton Barber, 250 Church St., New Haven. *Homeopathic Examination.* Derby, Nov. 9-10. Sec., Dr. J. H. Evans, 1408 Chapel St., New Haven.

FLORIDA: * *Examination,* Jacksonville, Nov. 29-30. Sec., Dr. Frank D. Gray, 12 N. Rosalind Ave., Orlando.

GEORGIA: *Examination.* Atlanta, Oct. 12-13. *Endorsement,* Atlanta, Oct. 14. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta.

GUAM: *Endorsement.* Agana, Last Friday of each month. Sec., Capt. C. K. Youngkin, Dept. of Public Health, Guam, % F.P.O. San Francisco, Calif.

HAWAII: *Examination,* Honolulu, Jan. 10-13. Sec., Dr. S. E. Doolittle, 881 S. Hotel St., Honolulu 53.

IDAHO: Boise, Jan. 10-12. Dir., Bureau of Occupational Licenses, Miss Estella S. Mullinex, State House, Boise.

INDIANA: *Examination,* Indianapolis, June 1949. Sec., Board of Medical Registration & Examination, Dr. Paul R. Tindall, 416 K. of P. Bldg., Indianapolis.

IOWA: * *Examination.* Des Moines, Dec. 6-8. *Endorsement.* Des Moines, Dec. 6. Sec., Dr. M. A. Royal, 506 Fleming Bldg., Des Moines.

KANSAS: Topeka, Dec. 15-16. Sec., Board of Medical Registration & Examination, Dr. J. F. Hassig, 905 N. 7th St., Kansas City.

KENTUCKY: *Examination,* Louisville, Dec. 13-15. Sec., Dr. Bruce Underwood, 620 S. 3rd St., Louisville 2.

LOUISIANA: *Examination.* New Orleans, Dec. Sec.-Treas., Dr. R. B. Harrison, 1507 Hibernia Bank Bldg., New Orleans 12. *Homeopathic Examination.* Baton Rouge, subject to call. Sec., Dr. F. H. Hardenstein, 715 Pere Marquette Bldg., New Orleans.

MAINE: Portland, Nov. 9-10. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Examination.* Baltimore, Dec. 14-17. *Endorsement,* At the discretion of the Board. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore. *Homeopathic Examination.* Baltimore, Dec. 7-8. Sec., Dr. J. A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: *Examination,* Boston, Nov. 16-19. Sec., Board of Registration in Medicine, Dr. G. L. Schadt, 413 E. State House, Boston.

MICHIGAN: * *Examination.* Lansing, Oct. 13-15. *Endorsement.* Oct. 12. Sec., Dr. J. E. McIntyre, 203 Hollister Bldg., Lansing.

MINNESOTA: Minneapolis, Oct. 19-21. Sec., Dr. J. F. DuBois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: *Reciprocity,* Jackson, Dec. 6. Exec. Officer, State Board of Health, Dr. Felix J. Underwood, Jackson.

MISSOURI: St. Louis, Oct. 25-27. Exec. Sec., Mr. John A. Hailey, P.O. Box 4, Jefferson City, Mo.

NEVADA: Carson City, Nov. 1. Sec., Dr. G. H. Ross, Industrial Bldg., Carson City.

NEW HAMPSHIRE: Concord, March 10. Sec., Board of Registration in Medicine, Dr. John S. Wheeler, 107 State House, Concord.

NEW JERSEY: *Examination.* Trenton, Oct. 19-22. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe, Oct. 11-12. Sec., Dr. V. E. Berchtold, 141 Palace Ave., Santa Fe.

NORTH CAROLINA: *Endorsement.* Wilson, Oct. 25. Sec., Dr. Ivan M. Procter, 226 Hillsboro St., Raleigh.

NORTH DAKOTA: *Examination.* Grand Forks, Jan. 4-7. Act. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Examination.* Columbus, Dec. 13-15. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA: * *Reciprocity,* Oklahoma City, Oct. 24-25. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

PENNSYLVANIA: *Examination.* Philadelphia, Jan., 1949. Act. Sec., Mrs. M. G. Steiner, 351 Education Bldg., Harrisburg.

SOUTH CAROLINA: *Endorsement.* Dec. 6. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA: * Pierre, Jan. 18-19. Sec., Dr. G. J. Van Heuvelen, Capitol Bldg., Pierre.

TEXAS: Fort Worth, Nov. 4-6. Sec.-Treas., Dr. M. H. Crabb, Medical Arts Bldg., Fort Worth.

UTAH: *Examination.* Salt Lake City, July. Sec., Dept. of Registration, Miss Rena B. Lounis, 324 State Capitol Bldg., Salt Lake City.

VERMONT: *Examination.* Burlington, Feb. Sec., Dr. F. J. Lawliss, Richford.

VIRGIN ISLANDS: *Examination,* Charlotte Amalie, Dec. 8-9. Comm., Dr. Christian R. Moorhead, Charlotte Amalie.

VIRGINIA: *Examination.* Richmond, Dec. 3-4. *Endorsement.* Dec. 3. Sec., Dr. K. D. Graves, 30½ Franklin Road, Roanoke.

WASHINGTON: * Seattle, Jan. Sec., Dept. of Licenses, Miss Virginia Wotherspoon, Olympia.

WISCONSIN: * Madison, Jan. 11-13, 1949. Sec., Dr. C. A. Dawson, Tremont Bldg., River Falls, Wis.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

DISTRICT OF COLUMBIA: *Examination,* Washington, Oct. 18-19. Sec., Dr. G. C. Ruhland, 4130 Municipal Bldg., Washington, D. C.

FLORIDA: *Examination.* Gainesville, Nov. 6. Final date for filing application is Oct. 25. Mr. M. W. Emmel, University of Florida, Gainesville.

IOWA: Des Moines, Oct. 12. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids.

MINNESOTA: *Examination.* Jan., April, June and Oct. Sec.-Treas., Dr. Raymond N. Bieter, 105 Millard Hall, Univ. of Minnesota, Minneapolis.

OKLAHOMA: Spring of 1949. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination,* Portland, Dec. Sec., Basic Science Examining Committee, Dr. C. D. Byrne, Univ. of Oregon, Eugene.

SOUTH DAKOTA: *Examination.* Vermillion, Dec. 3-4. Sec., Dr. G. M. Evans, Yankton.

WASHINGTON: Seattle, Jan. Sec., Dept. of Licenses, Miss Virginia Wotherspoon, Olympia.

WISCONSIN: *Examination.* Milwaukee, Dec. 4. Final date for filing application is Nov. 27. Sec., Prof. W. H. Barber, Scott & Watson Sts., Ripon.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1937 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

17:361-404 (May) 1948

Scalenus Anticus Syndrome: Consideration of Diagnosis and Treatment. N. Bograd and G. S. Peters.—p. 361.
Evidence of Contact Spread of Poliomyelitis. A. E. Casey.—p. 365.
Pregnancy in Rudimentary Horn with Case Report. T. J. Payne. —p. 367.
Observations on Caudal and Intravenous Analgesia in Obstetrics. K. N. Gold.—p. 369.

17:405-464 (June) 1948

Clinical Picture of Auricular Fibrillation. C. K. Weil.—p. 405.
Mental Ill-Health! Time to Immunize! Job for Education. J. Leese. —p. 410.
Treatment of Brill's Fever. J. T. Grimes.—p. 416.

American Heart Journal, St. Louis

35:689-872 (May) 1948

Studies on Coronary Circulation: III. Collateral Circulation of Heating Human and Dog Hearts with Coronary Occlusion. M. Prinzmetal, H. C. Bergman, H. E. Kruger, Lois L. Schwartz and others.—p. 689.
*Diagnosis of Mitral Insufficiency in Rheumatic Children. Ann G. Kuttner and M. Markowitz.—p. 718.
Relation of Unipolar Limb Leads to Precordial and Esophageal Leads. G. B. Myers and H. A. Klein.—p. 727.
New Electronic Method for Simultaneous Recording of Ballistocardiograph and Electrocardiograph. H. R. Brown Jr. and R. Pearson. —p. 756.
Seasonal Variations in Heart and Coronary Disease as Related to Various Environmental Factors. H. R. Brown Jr. and R. Pearson. —p. 763.
Note on Importance of Proper Technic in Recording of Precordial Electrocardiogram: Description of Important Source of Error. R. F. Ziegler.—p. 769.
Observations on Effects on Lungs of Respiratory Air Flow Resistance in Dogs with Special Reference to Vagotomy. S. Zinberg, G. Nudell, W. G. Kubicek and M. B. Visscher.—p. 774.
Measurement of Total Transverse Diameter of Heart by Direct Percussion. W. D. Stroud, M. W. Stroud III and D. S. Marshall.—p. 780.
Intensity and Duration of Action of Quinidine Sulfate in Auricular Fibrillation and Flutter as Measured by Rate of Circus Movement. R. Wegria.—p. 787.
Experiences with New Synthetic Analgesic, Amidone: Its Action on Ischemic Pains of Occlusive Arterial Diseases. R. J. Popkin.—p. 793.
Electrocardiographic Changes in Pulmonary Collapse Therapy: Artificial Pneumothorax. D. Feldman and C. Silverberg.—p. 800.

Mitral Insufficiency in Rheumatic Children.—The material analyzed by Kuttner and Markowitz was obtained from the records of patients who received convalescent care at a sanatorium for the care and study of children with rheumatic heart disease. Children 6 to 15 years of age, with histories of one or more attacks of rheumatic fever or chorea, were observed for various lengths of time ranging from two months to two years. Following discharge, each child was seen annually at the after-care clinic. The patients included in this study were followed for an average of eight years. The records of 315 rheumatic patients were selected for study. Group 1 consisted of 171 patients classified as having potential and possible rheumatic heart disease. These patients had soft, poorly transmitted, apical systolic murmurs and no evidence of cardiac enlargement. Group 2 consisted of 144 given a diagnosis at the time of discharge of mitral insufficiency. Of the 144 patients with mitral insufficiency, in 69 organic heart disease has developed. Of these, 13 died as a result of their rheumatic infection and 7 succumbed to bacterial endocarditis. Ninety-two of these 144 patients had a history of multiple attacks prior to the period of observation and 28 had rheumatic recurrences following sanatorium care. Of the 171 patients with potential and possible rheumatic heart disease, in 22 evidence developed of organic heart disease. None of the children in this group died. Fifty-two of the 171 patients had a history of multiple attacks prior to the period of observation and 12 had rheumatic recurrences following sanatorium care. The striking difference between the two groups in this progression of the disease and the mortality rate indicates that the intensity of the murmur is of prognostic significance. The diagnosis of mitral insufficiency, based on a loud blowing apical systolic murmur, is justified in children, even in the absence of demonstrable cardiac enlargement.

American Journal of Pathology, Ann Arbor, Mich.

24:451-728 (May) 1948

Metastatic Calcification Produced in Dogs by Hypervitaminosis D and Haliphagia. R. M. Mulligan and F. L. Strickler.—p. 451.
Cicatrizing Enteritis (Regional Ileitis) as Pathologic Entity: Analysis of 120 Cases. S. Warren and S. C. Sommers.—p. 475.
Hepatic and Renal Injury with Calcium Deposits and Cirrhosis Produced in Rats by Pyridine. J. H. Baxter.—p. 503.
Biliary Xanthomatosis (Xanthomatous Biliary Cirrhosis). H. E. MacMahon.—p. 527.
Cytologic Studies with Phase Microscope: I. Formation of "Blisters" on Cells in Suspension (Potocytosis), with Observations on Nature of Cellular Membrane. H. U. Zollinger.—p. 545.
Id.: II. Mitochondria and Other Cytoplasmic Constituents under Various Experimental Conditions. H. U. Zollinger.—p. 569.
Melanomas of Childhood. Sophie Spitz.—p. 591.
Lesions of Schistosomiasis Japonica. M. M. Bracken, W. R. Bailey Jr., and H. M. Thomas Jr.—p. 611.
Significance of Local Vascular Phenomena in Production of Ischemic Necrosis in Skeletal Muscle. J. W. Harman.—p. 625.
Periodic Acid Routine Applied to Kidney. J. F. A. McManus.—p. 643.
Epithelium-like Inclusions in Heart. S. M. Rabson and L. J. Thill. —p. 655.

Annals of Internal Medicine, Lancaster, Pa.

28:887-1074 (May) 1948

Emetine Toxicity In Man: Studies on Nature of Early Toxic Manifestations, Their Relation to Dose Level, and Their Significance in Determining Safe Dosage. G. Klatskin and H. Friedman.—p. 892.
*Experience with Schemm Regimen in Treatment of Congestive Heart Failure. A. A. Newman and H. J. Stewart.—p. 916.
Clinical Aspects of Carcinoma of Cecum and Ascending Colon: Report of 60 Cases. C. H. Brown, J. R. Colvert and B. E. Brush.—p. 940.
Course of Beriberi Heart Disease in American Prisoners of War in Japan. R. J. Alleman and G. H. Stollerman.—p. 949.
*Myocarditis in Instances of Pneumonia. O. Saphir and G. D. Amromin. —p. 963.
*Role of Hormones in Treatment of Obesity. M. M. Kunde.—p. 971.
Clinical and Electrocardiographic Study of Paroxysmal Ventricular Tachycardia and Its Management. G. R. Herrmann and M. B. Hejtmancik.—p. 989.
Appendicitis and Upper Respiratory Infection: Report of 18 Cases at Sea. G. L. Calvy.—p. 998.
Friedländer Bacillus Meningitis: Report of 7 Cases with 2 Recoveries. S. S. Jacob and F. H. Top.—p. 1003.
Adreno-Sympathogenic Heart Disease (Neurohormonal Factors in Pathogenesis and Treatment). W. Raab.—p. 1010.

Schemm Regimen in Congestive Heart Failure.—Newman and Stewart analyzed the diuretic effect of the Schemm regimen, which consists of a low sodium, neutral and acid ash diet, in patients with congestive heart failure. Many cases were found unsuitable for trial with the Schemm regimen. Of 30 cases originally studied, only 9 could be considered suitable for analysis, and in at least half of these complications developed which interfered at some time with the proper maintenance of the regimen. Ascites proved to be the most difficult manifestation of heart failure to treat. Seven of the 9 patients fared better on the usual regimen of restricted salt and limited fluids with frequent administration of mercurophylline than they did on the Schemm regimen when fluids were forced and no mercurial diuretics were given. The authors say that in their experience the Schemm regimen has not been successful as a diuretic procedure in the treatment of heart failure.

Myocarditis in Pneumonia.—Saphir and Amromin studied by means of multiple microscopic sections the hearts of 67 patients with bronchopneumonia, involving at least one lobe of the lungs. Twenty-six of these revealed inflammatory changes sufficient to warrant the term "myocarditis." Fifteen were classified as acute myocarditis, 3 as acute serous, and 8 as subacute myocarditis. The outstanding clinical criteria pointing to the diagnosis were found to be: disproportion between the pulse rate and the temperature, drop in the arterial blood pressure, cyanosis out of proportion to the apparent

pulmonary involvement and unexpected death. Six of these 26 patients exhibited electrocardiographic abnormalities. Emphasis was placed on the necessity of examining multiple sections of the myocardium either to establish or to disprove a diagnosis of myocarditis.

Hormones in Treatment of Obesity.—This report by Kunde is based on the study of 50 patients with obesity. All had been referred for endocrine treatment either because of debilitating overweight, presumably due to some vague endocrinopathy, or because of some specific endocrine dysfunction with which the overweight was associated. The author stresses that no hormones or gland products are necessary adjuncts in the treatment of any type of obesity, excepting hypothyroidism. Thyroid hormones should be administered solely for the correction of a specific hypothyroidism. When this is properly accomplished, the obesity will take care of itself or it should be managed by dietary regulation. The use of thyroid extract in patients with adiposity but with no hypothyroidism, solely for the purpose of attempting to effect weight loss by stimulating metabolism, is fraught with disappointment and failure. Such overweight patients soon manifest the symptoms of severe induced hyperthyroidism with little or no weight loss. A high protein, low fat, low carbohydrate diet, supplemented with vitamins and minerals, and with no calculation of caloric values or administration of any known hormones, results in satisfactory weight reduction in all known types of obesity. Endocrine obesity is a term which is misleading in that it conveys to the obese patient a false idea, suggesting that his obesity is due to some specific endocrine glandular deficiency which can be corrected by substitution endocrine, or hormone therapy. This causes the patient to seek needless endocrine medication, whereas dietary measures and reeducation of faulty food habits are the true solutions to correction of obesity.

Arizona Medicine, Phoenix

5:1-120 (May) 1948

Management of Chronic Bronchopulmonary Suppuration. P. C. Samson.—p. 29.
Diagnosis and Treatment of Bowel Obstructions. P. Thorek.—p. 38.
Chronic Coccidioidal Meningitis: Case History. I. Frank.—p. 41.
*Effect of Protein Deficiency in Average Diets. H. V. Super.—p. 46.
Early Ambulation and Decreased Incidence of Post-Operative Complications. H. A. Barnes.—p. 50.

Protein Deficiency in Average Diets.—Soper studied for ten years 308 persons ranging from 4 to 82 years. The persons were given a complete physical examination to rule out definite medical and surgical conditions and only those who presented no obvious disease were included in this series. They were living an average life and many believed they were eating adequately, but thought it quite "un-American" to eat meat for breakfast. The occupations were largely those of the so-called white collar class and housewives, but also included a few heavy physical workers. Typical symptoms included loss of appetite, a need for eight to twelve hours of sleep, a drowsiness from arising till coffee or a cold shower had been taken. They hurried to work. Many had a feeling of well-being until about 9:30 or 10 o'clock, when a let-down occurred and a snack was needed. Lunch was eaten usually in a hurry and the patient felt fairly well till about 2 o'clock, when again he felt let down, which progressed till quitting time. Many felt so exhausted that on arriving home they had to sit and rest and often napped till time to prepare or eat dinner. Some felt best after dinner and others were so tired they felt they had to go to bed so as to be able to go to work the next morning. The author insists on a large protein serving for breakfast. It was found that any kind of lean meat, fish or fowl such as steaks, ham, pork, pork chops, lamb chops, mutton, chicken, fish, rabbit, turkey, liver or ground meats, or roasts, or cold meats, if eaten in large amounts, would suffice. Bacon has only slight value. The author stresses that the use of large quantities of meat protein up to 3 to 4 Gm. per kilogram of body weight, especially for breakfast, can do far more for the general health and strength of these patients than prolonged therapy with vitamins, iron, liver, minerals and such.

Connecticut State Medical Journal, Hartford

12:403-506 (May) 1948

Diagnosis of Brucellosis. W. W. Spink.—p. 406.
Fundus Changes in Blood Dyscrasias. E. M. Blake.—p. 410.
Practical Approach to Problem of Epidemic Ringworm of Scalp. S. M. Peck.—p. 413.
Painless Labor with Heavy Nupercaine. M. L. Berlove and F. L. Herrick.—p. 417.
Puerperal Subperitoneal Hematoma: Case Report. F. W. Shull and H. Thoms.—p. 419.
Medicine and the Future. L. S. Goin.—p. 422.

12:507-606 (June) 1948

Future of Our Voluntary Hospitals. R. P. Shaw.—p. 509.
Use of Vaginal Smear in Diagnosis of Cancer. H. Ulfelder.—p. 513.
Coronary Artery Disease in Women Under Age of Thirty. (A report of 2 Cases). P. J. Steincrohn.—p. 515.
Penicillin in Treatment of Syphilis. F. W. Reynolds.—p. 518.
Psychoneuroses: Clinical Evaluation by Internist. B. V. White.—p. 522.
Infectious Mononucleosis: A Report on 24 Cases. N. E. Creature, I. B. Akerson and Margaret M. Flanagan.—p. 526.
Utilization of a University Cancer Clinic for Teaching Purposes. M. Taffel.—p. 532.
Government and Medicine. J. R. Miller.—p. 535.

Diseases of Chest, Chicago

14:317-474 (May-June) 1948

Treatment of Patent Ductus Arteriosus. W. S. Conklin.—p. 317.
Closure of Cavities in Pulmonary Tuberculosis Produced by Immobilization of Both Lungs. J. H. Cullen, R. K. Myers, A. L. Barach and G. F. Herben.—p. 345.
Pulmonary Heart Disease. W. A. Sodeman.—p. 360.
Role of Bronchoscopy in Clinical Medicine and Surgery. A. Q. Penta.—p. 366.
Demand Valve for Administration of Aerosols of Penicillin and Streptomycin. M. S. Segal, L. L. Levinson and J. F. Brakey.—p. 386.
Tumors of Anterior Mediastinum: Report of 6 Cases. M. S. Lloyd.—p. 396.
Combined Thoracoplasty. G. Maurer.—p. 415.
Cardiospasm with Associated Pulmonary Disease. T. G. Heaton.—p. 425.
Bronchial Adenoma. W. E. Howes.—p. 427.
Bronchiectasis in Children. A. Chattas.—p. 437.
Present Status of Streptomycin in Tuberculosis. K. H. Pfuetze and W. M. Ashe.—p. 446.

Georgia Medical Association Journal, Atlanta

37:121-166 (April) 1948

Management of Injuries of Elbow Joint. C. Sandison.—p. 121.
Observations on Fitting of Artificial Limbs. B. W. Harris.—p. 127.
Use of Novocain and Oil in Treatment of Low Back Injuries. W. W. Turner.—p. 134.
Newer Concepts in Treatment of Cirrhosis of Liver. E. A. Allen.—p. 136.
Pigmented Lesions of Eye and Adnexae. F. P. Calhoun Jr.—p. 140.
Nature's Disturbances and Cures in Ophthalmology. E. S. Osborne.—p. 142.
How and Why of Visual Tests. H. R. Perkins.—p. 145.
The General Practitioner and His Opportunities. V. Johnson.—p. 149.

Indiana State Medical Assn. Journal, Indianapolis

41:487-572 (May) 1948

Vascular Changes of Eye Associated with Diabetes Mellitus. C. B. McFarland.—p. 487.
Styes: Role of Nutrition in Etiology and Treatment. W. M. Cockrum, H. D. Lynch, H. C. Slaughter and W. E. Austin.—p. 489.
Cross Cylinder in Refraction. M. Cuthbert.—p. 491.
Hemorrhages of Retina: Newer Treatment. C. W. Rutherford.—p. 494.
Headache. C. L. Mahoney.—p. 496.
Periorbital Cellulitis: Report of 4 Cases. W. R. Hickman.—p. 501.

41:591-676 (June) 1948

*Rocky Mountain Spotted Fever in Indiana: Recent Advances in Therapy. H. H. Muntz and I. Salkin.—p. 591.
Treatment of Diabetic Coma at Indianapolis General Hospital. F. B. Peck.—p. 595.
Fracture of Shaft of Femur. E. B. Mumford.—p. 599.
Brucellosis: Résumé of Present Concepts with Special Reference to Chronic Illness. H. J. Harris.—p. 603.

Rocky Mountain Spotted Fever.—According to Muntz and Salkin Rocky Mountain spotted fever has been reported in 47 of 48 states and accounts for approximately 140 deaths annually in the United States. The disease increases in severity as one moves westward. The average figures for mortality are 25 per cent for Eastern states, 50 per cent for the Western states and 75 per cent for the Far West. On the basis of a survey of the disease in Indiana, the authors stress that Rocky Mountain spotted fever is endemic in Indiana. One hundred and ten cases have been reported in the ten-year period between 1937 and 1947. The mortality rate at the Indiana University Medical Center before para-aminobenzoic acid therapy was

33 per cent (8 deaths in 24 cases). In 8 patients treated with para-aminobenzoic acid, 1 death occurred. The disease is most prevalent in June, July and August. Any acute disease which begins with fever, chills, severe headache, pain in the bones and muscles and a macular eruption which becomes petechial after recent contact with ticks should be strongly suspected of being Rocky Mountain spotted fever. The authors believe all patients with Rocky Mountain spotted fever should be treated with para-aminobenzoic acid. Routine symptomatic care and antibiotic drugs are valuable adjuncts to prevent secondary infection in the debilitated patient. The specific vaccine for Rocky Mountain spotted fever should be considered as a possible method of prophylaxis.

Journal of Bone and Joint Surgery, Boston

30B:229-404 (May) 1948

Paraplegia in Cervical Spine Injuries. R. Barnes.—p. 234.
Paraplegia in Hyperextension Cervical Injuries with Normal Radiographic Appearances. A. R. Taylor and W. Blackwood.—p. 245.
Pressure at Cervico-Brachial Junction: Operative and Anatomical Study. E. D. Telford and S. Mottershead.—p. 249.
Fatigue Fractures of Fibula. H. J. Burrows.—p. 266.
Management of Acute Circulatory Failure in Injured Limb. D. L. Griffiths.—p. 280.
*Clinical Diagnosis of Fat Embolism. P. H. Newman.—p. 290.
Plastic Splints and Appliances in Orthopedic Surgery. W. Herschell and J. T. Scales.—p. 298.
*Traumatic Uraemia: Collective Review. E. M. Darmady.—p. 309.
Movements of Bones and Joints: I. Fundamental Principles with Particular Reference to Rotation Movement. M. A. MacConaill. —p. 322.

Clinical Diagnosis of Fat Embolism.—According to Newman fat embolism occurs in a high percentage of all cases of injury. It is a relatively frequent complication of fractures of the long bones in civilian accidents as well as battle casualties. The diagnosis can usually be established by the clinical features together with certain physical signs which must, however, be sought deliberately. Important clinical features are mental changes such as failure to cooperate, restlessness, delirium, stupor, alternation of coma with full consciousness, petechial hemorrhages in the conjunctiva and skin, particularly in the supraclavicular regions, and typical changes in the retina. Evidence is still conflicting as to whether the fat arises by embolism from an injured bone or by general metabolic disturbance. The fat is harmful not so much by reason of mechanical obstruction of vessels as by erosion and rupture of the vessel wall due to the liberation of fatty acids. Preventive treatment includes protection from long journeys over rough roads and care to avoid unnecessary manipulation. It appears to be of some value but no satisfactory specific treatment is yet available for the established case. Ligation of the profunda vein as a means of arresting venous drainage from the area of the femur has been tried in 2 patients, one of whom recovered and the other died.

Traumatic Uremia.—Darmady believes that traumatic uremia is of particular significance to orthopedic surgeons so far as this complication is responsible for high mortality in severe injury, crushing injury, traumatic shock, gun shot wounds, incompatible blood transfusions and the misuse of tourniquets. The association between muscle injury and renal failure is reviewed. The syndrome of the "crush kidney," which at first was thought to be the result of deposition of myohemoglobin in the renal tubules, is almost certainly due to the association of many factors all of which lead to alteration of the renal circulation and renal ischemia. Ischemia of the kidney combined with deposition of pigment and hemolysis of blood causes a high mortality in animals. This may account for the serious prognosis in man where there is both shock and hemolysis. Disturbance of water balance, allergic phenomena and chemical nephrotoxic action are discussed as other possible etiologic factors. Necropsies revealed that probably the only characteristic change of the syndrome of traumatic uremia is in the kidney itself, which is increased in weight. The greatest changes occur in the loops of Henle. There is a wide variety of casts which tends to obscure the tubular degeneration. One of the most interesting features is the occurrence of venous thrombi in the boundary zone associated with rupture of the tubules into the veins. A plea is made for early clinical recognition of the syndrome with its characteristic features, such as vomiting, oliguria, hypertension with rapid and pronounced rise of blood urea or nonprotein nitrogen. Important aspects of treatment such as correction of electrolyte balance, management of water metabolism, use of sodium sulfate, artificial kidney, peritoneal dialysis and renal decapsulation are discussed. The dangers of excessive intravenous infusion are emphasized.

Journal of Clin. Endocrinology, Springfield, Ill.

8:271-344 (April) 1948

Interstitial Tissue of Human Hermaphrodite. E. Van Campenhout and E. Witschi.—p. 271.
Adrenal and Testicular Deficiency: Comparison Based on Similarities in Androgen Deficiency, Androgen and 17-Ketosteroid Excretion, and on Differences in Their Effects on Pituitary Activity. E. P. McCullagh, T. W. Schneider, W. Bowman and M. B. Smith.—p. 275.
Analogies Between Urinary 17-Ketosteroids and Urinary "Estroids," as Determined Microchemically. W. T. Salter, Frances D. Hunsu and M. Jane Oesterling.—p. 295.
Alkaline Phosphatase and Glycogen in Human Endometrium. J. P. Arzac and E. Blanchet.—p. 315.
Use of Globin Insulin in Addison's Disease Associated with Insulin-Sensitive Diabetes. W. L. Lowrie, W. E. Redfern and D. P. Foster. —p. 325.
Diabetes in a Dwarf: Case Report. H. Schreier and I. Lewenter. p. 332.

Journal of Clinical Investigation, Boston

27:299-388 (May) 1948

Effects of Hypoxia and Hyperpnoea on Perception of Thermal Cutaneous Pain. J. Stokes III, W. P. Chapman, and L. H. Smith.—p. 299.
*Use of Concentrated Human Serum Albumin in Treatment of Cirrhosis of Liver. H. G. Kunkel, D. H. Labby, E. H. Ahrens Jr. and others. —p. 305.
Complement Content of Human Serums with Especial Reference to Malaria. Anna Dean Dulaney.—p. 320.
Lung Function Studies: I. Rate of Increase of Arterial Oxygen Saturation During Inhalation of 100 Per Cent O2. W. S. Fowler and J. H. Comroe Jr.
Effect of Spinal Anesthesia on Renal Ischemia in Congestive Heart Failure. R. Mokotoff and G. Ross.—p. 335.
Changes in Serum Proteins in Patients with Experimentally Induced Infectious Hepatitis. W. P. Havens Jr. and T. L. Williams.—p. 340.
Changes in Cerebrospinal Fluid Pressure Under the Infusion of Normal Saline. F. F. Foldes and Julia G. Arrowood.—p. 346.
Blood and Extracellular Fluid Studies in Chronic Malnutrition in Infancy. F. Gellhan.—p. 352.
Studies on Gangrene Following Cold Injury: IX. Effect of Rutin and Other Chemical Agents on Course of Experimental Frostbite in Rabbits. F. A. Fuhrman and J. M. Crismon.—p. 364.
Kidney Function in Adrenal Insufficiency. Christine Waterhouse and E. H. Krutmann.—p. 372.
Studies on Pain: Investigation of Some Quantitative Aspects of Dol Scale of Pain Intensity. J. D. Hardy, H. C. Wolff and Helen Goodell.—p. 380.

Concentrated Human Serum Albumin in Hepatic Cirrhosis.—Kunkel and his associates report the results of albumin therapy in 17 patients with severe hepatic disease. All but 2 of them had ascites at the time when albumin was first administered. In 9 of 15 patients with fluid retention who were treated, a rapid loss of edema and ascites occurred. Five others showed a delayed loss of ascites. In those patients whose diuretic response to albumin was immediate, a beneficial course of events was rapidly initiated; loss of protein into ascitic fluid ceased, dietary protein intake increased, and positive nitrogen balance resulted. Such treatment carried seriously ill patients through the early critical period of their disease until such time as dietary and liver extract therapy had an opportunity to take effect. The amount of albumin needed to produce a loss of ascites was extremely variable, ranging from 4 to 80 units. Patients with evidence of portal obstruction, a high antidiuretic titer in the urine or long-standing ascites proved unresponsive to therapy. Patients with particularly severe hepatic disease and low plasma albumin levels following infectious hepatitis responded most readily to therapy. Patients having alcoholic and nutritional cirrhosis with a short period of ascites also responded to relatively small doses of albumin. Permanently beneficial results were obtained in 6 of 7 patients with the nutritional type of cirrhosis. Two of these patients required a second short course of therapy. Patients with postnecrotic cirrhosis after infectious hepatitis and biliary cirrhosis showed only a temporary response, and 4 of these patients eventually died. Evidence was presented for certain specific effects of serum albumin on dietary intake and nitrogen balance which may be of greater importance in the results obtained than its osmotic properties.

Journal Industrial Hygiene & Toxicology, Baltimore

30:145-210 (May) 1948

Fume Exposure in Manufacture of Alumina Abrasives from Bauxite. C. M. Jephcott, J. H. Johnston and G. R. Finlay.—p. 145.
*Effect of Use of Calcined Alumina in China Biscuit Placing on Health of Workmen: Field Study in Group of Pottery Workers in North Staffordshire. A. Meiklejohn and W. W. Jones.—p. 160.
X-Ray Diffraction Analysis of Crystalline Dusts. H. P. Klug, L. Alexander and Elizabeth Kummer.—p. 166.
Influence of Particle Size in Dust Exposure. T. Hatch and W. C. L. Hemeon.—p. 172.
Retention of Air-Borne Particulates in Human Lung. H. D. Landahl and R. G. Hermann.—p. 181.
Toxicology of 1,2-Dichloropropane (Propylene Dichloride): Effects of Repeated Exposures to Low Concentration of Vapor. L. A. Heppel, B. Highman and E. G. Peake.—p. 189.
Hair Loss in Neoprene Manufacture. W. L. Ritter and A. S. Carter. —p. 192.
Medical Aspects of Maximum Allowable Concentrations: Benzene. Harriet L. Hardy and H. B. Elkins.—p. 196.
Use of Adsorbents for Protection Against Ammonia. J. C. Goshorn. —p. 201.
Determination of Chlorinated Hydrocarbons in Air. J. P. Fahy. —p. 205.

Effect of Calcined Alumina on Health of the Workmen.—Meiklejohn and Jones point out that inhalations of small amounts of suitably prepared pure aluminum metal, for short periods each day, have been used to inhibit toxic effects of silica in the lung and thereby delay, if not altogether prevent, the production of silicotic fibrosis. It occurred to the authors that a practical field test of the efficacy of one form of alumina in the treatment and prevention of silicosis had been in progress, over a period of years, among certain workmen in the pottery industry employed in the "placing" of china ware for the biscuit firing. Until 1929 finely powdered calcined flint was the medium in general use for this process, but later there was a gradual change over to the use of calcined alumina (Al_2O_3). The authors review observations on 52 china biscuit placers who had previously been examined by the medical board. All had considerable previous exposure to flint, followed by daily exposure to alumina varying from two to sixteen years. All the workmen were convinced that alumina produced a dustier atmosphere than flint, but all were agreed that alumina did not irritate the nose and throat or induce the feeling of stuffiness on the chest so familiar to them with flint. The old fear of the "dust" had gone. Even so complaints of cough, expectoration and dyspnea were as frequent as before. When flint was the medium the china biscuit placer was pale, often haggard and listless, but now he appeared natural in complexion, robust and active. These workers were reexamined. It was found that although this group of workmen were daily exposed to finely powdered alumina in a greater intensity and over a considerably longer period than is possible by existing methods of aluminum prophylaxis and therapy, not only did new cases of silicosis occur but known cases advanced. The authors think that ten or twenty years must elapse before any authoritative opinions on the subject can be expressed, and that reports based on short term observations should be treated with circumspection.

Journal-Lancet, Minneapolis

68:169-216 (May) 1948

Asthmatic Children. R. Bowen.—p. 169.
Common Endocrine Problems in Childhood. R. B. Tudor and H. H. Groskloss.—p. 178.
Normal Electrocardiograph in Children. Evelyn S. Harris and P. F. Dwan.—p. 183.
Preliminary Report on Association of Growth Failure and Poliomyelitis. N. N. Litman and J. F. Bosma.—p. 185.
Peritonitis in Newborn of Intra-Uterine Origin. L. F. Richdorf and L. H. Cady.—p. 188.
Subdural Hematoma in Infants. W. R. Heilig, R. B. Tudor and E. S. Platou.—p. 192.
Well-Water Methemoglobinemia in Infants: Its Occurrence in Rural Manitoba and Ontario. H. Medovy.—p. 194.
Arteriosclerosis in Nine Year Old Child. J. L. Gedgoud and J. P. Tolman.—p. 197.
Use of Plastic Nipple Shields for Lactating Breast. C. H. McKenzie. —p. 199.
Value of Psychiatric Consultant to University Student Health Service. Harriet Hunter and Mary L. Gorton.—p. 201.
Comparative Studies in Tuberculosis and Histoplasmosis Among 2000 Students Entering Pennsylvania State College September 1947. E. S. Krug and H. R. Glenn.—p. 206.

J. Neuropathology & Exper. Neurology, Baltimore

7:123-234 (April) 1948

Studies in Treatment of Experimental Hydrocephalus. F. D. Ingraham, D. D. Matson, E. Alexander Jr. and R. P. Woods.—p. 123.
Carcinomas of Tongue in Monkeys and Pathologic Changes in Central Nervous System. H. Kluver and A. Weil.—p. 144.
Golgi Apparatus in Autonomic Ganglion Cells and Peripheral Neuroglia and Its Modification Following Stimulation and Induced Hypertension. N. M. Sulkin and A. Kuntz.—p. 154.
Subcortical Changes in Cerebral Concussion. E. A. Spiegel, M. Spiegel-Adolf, and H. T. Wycis.—p. 162.
*Cerebrospinal Fluid: Its Origin, Nature and Function. G. B. Hassin, —p. 172.
Second Motor Cortex In Monkey (Macaca Mulatta). O. Sugar, J. G. Chusid and J. D. French.—p. 182.
*Kernicterus: Review with Report of Findings in Study of 7 Cases. P. F. L. Becker and P. Vogel.—p. 190.
Histometabolic Changes and Neuropathologic Selectivity in Light of Recent Investigations (Histometabolic Dysergia). L. Roizin.—p. 216.

Cerebrospinal Fluid.—The observations presented by Hassin on the complex problem of the origin, absorption and circulation of the cerebrospinal fluid are based chiefly on neuropathologic observations, experimental data being referred to only for comparison. He concludes that the cerebrospinal fluid represents the tissue fluids of the brain. The contents of the Virchow-Robin spaces which originate in the tissue fluids and which are discharged into the cerebral ventricles and the subarachnoid spaces are a part of the cerebrospinal fluid. The absorption of the cerebrospinal fluid is effected not through the villi or pacchionian bodies but through the perineurial spaces of the cranial nerves and spinal roots. The function of the choroid plexuses is not to secrete fluid but to excrete or eliminate from it noxious substances and to make it absorbable by the perineurial spaces. The cerebrospinal fluid is a lymph of the central nervous system, for it carries away its waste. There is no circulation of the cerebrospinal fluid under normal conditions. The collapsing and expanding movements of brain and spinal cord represent the forces that facilitate removal of the spinal fluid. The Virchow-Robin spaces represent the hematoencephalic barrier.

Kernicterus.—Becker and Vogel describe 7 cases of kernicterus, all of which were associated with erythroblastosis fetalis. The condition was confirmed by serologic and histologic studies. In cases 1, 2, 3, 5 and 7 the infants were Rh positive and the mother Rh negative with anti-Rh agglutinins. In case 4, the erythroblastosis was presumably due to the A factor. In case 6, the erythroblastosis was due to the Rh" factor. In 5 cases jaundice appeared during the first day of life; postmortem studies disclosed the discoloration to be present most frequently in the hippocampus, basal ganglions, midbrain, medulla and floor of the fourth ventricle. In regions grossly bile stained the nerve cells were shrunken and stained readily with eosin, some containing dark-staining nuclei. Some nerve cells displayed poorly stained cytoplasm and vacuolization. Extramedullary erythropoiesis, chiefly in the liver and spleen, and visceral hemorrhages were other anatomic findings.

Michigan State Medical Society Journal, Lansing

47:457-576 (May) 1948

Medicine and the Future. L. S. Goin.—p. 505.
Part of General Practitioner in Management of Vesical Neck Obstruction. F. E. B. Foley.—p. 509.
Unusual Forms of Rheumatic Pain. R. L. Cecil.—p. 516.
*Diagnosis and Treatment of Scabies. E. A. Hand.—p. 519.

Diagnosis and Treatment of Scabies.—Hand says that the normal decrease in scabies expected in the summer of 1946 did not occur. This was the result of the demobilization of infested army and navy personnel, pouring fresh scabies into the civilian population. The summer of 1947 saw the normal decrease, but the disease is again on the increase. Friedman noted that the acarus could easily be demonstrated by the scrape and smear method, and also that the diagnosis could be made by finding acarus eggs filled with embryo or empty, skeletal parts of the acarus, the larvae, and the scybala as well as from the adult acarus. Scabies should be suspected in all cases of furunculosis, as this often masks the underlying scabies. This is also true of ecthyma, pyoderma and impetigo in children. The following

areas should always be examined: the webs of the fingers, the anterior portion of the wrist, the inner and posterior part of the elbows, the anterior axillary folds, the nipples and breasts in women, the navel and abdomen, the shaft and glans penis in the circumcised, the penis shaft to the external rim of the foreskin in the uncircumcised, the scrotum, the buttocks, and the knees, ankles and toes. Though scabies is more common in the poor and unclean, it is found in all classes and in all periods of life. Next to avoidance of those infested, frequent bathing is the best prophylaxis. Sulfur has been used in many forms, but benzyl benzoate is the treatment of choice for scabies.

Minnesota Medicine, St. Paul

31:451-608 (May) 1948

The Drug Addict. E. M. Hammes.—p. 481.
Common Methods of Inguinal Hernia Repair: Comparison of Recurrence Rates. D. Sanderson and C. O. Rice.—p. 485.
Hemostasis in Tonsillectomy. G. M. A. Fortier.—p. 493.
Certain Factors Influencing Survival and Death in Coronary Artery Disease. F. A. Willius.—p. 497.
*Cold Prevention Study: Influenza Vaccine for Prevention of Common Cold. D. W. Cowan and H. S. Diehl.—p. 504.

Prevention of Cold.—The study reported by Cowan and Diehl was conducted at the request of the Commission on Influenza of the Office of the Surgeon General, U. S. Army. The experimental subjects were students of the University of Minnesota. A controlled study indicates that influenza vaccine A and B is of no value for the prevention of the common cold. The subjects who received influenza vaccine reported more reactions than the control group.

Nebraska State Medical Journal, Lincoln

33:153-188 (May) 1948

Role of General Practitioner in State and National Health. A. C. Sudan.—p. 155.
Some Deleterious Results of Rest in Bed After Orthopedic Operations. R. K. Ghormley.—p. 160.
Chronic Residuals of Brain Injury. J. A. Aita.—p. 163.
Unusual Complication Encountered in Removal of Large Retroperitoneal Ganglioneuroma. J. W. Gatewood, L. D. McGuire, A. C. Johnson and H. M. McCarthy.—p. 170.
Lasting Results Following Internal Urethrotomy for Urethral Stricture. E. Davis and L. W. Lee.—p. 173.
Cryotherapy (Dry Ice) in Treatment of Skin Diseases. W. E. Kelley.—p. 175.
Principles of Early Management of Hand Injuries. J. E. M. Thomson.—p. 177.

33:189-224 (June) 1948

Surgical Lesions of Pancreas. W. H. Cole.—p. 195.
Digitalis Derivatives. M. C. Andersen.—p. 203.
Symposium on Low Back Pain. Medical Considerations. R. A. Moser.—p. 205.
Neurologic Aspects of Low Back Pain. G. A. Young.—p. 206.
Gynecologic Aspects of Low Back Pain. J. J. Freymann.—p. 208.
Low Back Pain—Orthopedic Aspects. W. R. Hamsa.—p. 210.

New England Journal of Medicine, Boston

238:723-754 (May 20) 1948

*Portacaval Shunts in Treatment of Portal Hypertension with Special Reference to Patients Previously Operated Upon. R. R. Linton.—p. 723.
Salmonella Osteomyelitis of Spine Associated with Abdominal Aortic Aneurysm. K. R. Dehlinger.—p. 728.
*Bone and Joint Pain in Leukemia, Simulating Acute Rheumatic Fever and Subacute Bacterial Endocarditis. M. Aisner and T. B. Hoxie.—p. 733.
Orthopedic Surgery: II. Growth and Inequality of Leg Length in Poliomyelitis. J. S. Barr.—p. 737.
Empyema of Right Pleural Cavity.—p. 743.
Acute Glomerulonephritis, Acute Pulmonary Edema.—p. 746.

Portacaval Shunts in Portal Hypertension.—Linton presents 4 cases in 3 of which the results obtained in the treatment of portal hypertension, secondary to an extrahepatic portal bed block (Banti's syndrome), by the formation of portacaval shunts were encouraging, since none of the patients with satisfactory shunts has bled since they were performed. The most satisfactory portacaval shunt seems to be an end-to-side suture type of splenorenal anastomosis performed at the same operation at which the spleen is removed. In some patients who have had previous splenectomies it may be possible to perform other types of portacaval shunts, such as a superior mesenteric vein to inferior vena cava or inferior mesenteric vein to left ovarian vein. Two patients have gone twenty-two and fourteen months since the shunts were formed without evidence of esophagogastrointestinal hemorrhages. A direct portacaval anastomosis was not possible in 3 of these cases because of a cavernomatous transformation of the portal veins. It is believed that a surgeon should not do a splenectomy in a case of portal hypertension unless he is prepared to do a splenorenal anastomosis at the same operation, since this may be the only opportunity to construct a satisfactory shunt. A longer period of observation is necessary to determine whether the portal hypertension and the tendency to esophagogastrointestinal hemorrhages have been permanently influenced.

Pain in Leukemia Simulating Rheumatic Fever or Endocarditis.—Aisner and Hoxie report 4 cases of acute lymphatic leukemia, 3 of which presented signs and symptoms simulating those of acute rheumatic fever and 1 simulating those of subacute bacterial endocarditis. The authors discuss certain pitfalls and aids in the differential diagnosis between acute rheumatic fever and acute lymphatic leukemia. Complete examination of the blood should be performed routinely in all cases presenting bone or joint pains. The findings that point to the diagnosis of lymphatic leukemia rather than of acute rheumatic fever are leukopenia persistent in the presence of an active clinical course, leukopenia or leukocytosis associated with an increase in the percentage of lymphocytes and bone changes on roentgen examination. The authors enumerate the various bone changes in leukemia that are visible by roentgen study and stress the differential diagnostic importance of other disorders that cause bone and joint pain in young persons.

New Orleans Medical and Surgical Journal

100:491-538 (May) 1948

Poliomyelitis. B. J. Aymond.—p. 491.
Meningitis: Recent Advances in Therapy. C. J. Tripoli and W. G. Unglaub.—p. 492.
Peritoneoscopy: Analysis of Its Use in 69 Cases. W. J. Hollis and W. H. Brown.—p. 498.
Acute Mastoiditis: Secondary to Fracture of Mastoid. C. Vedrenne and J. R. Hays.—p. 504.
Dicumarol: Use of Dicumarol in Prevention and Treatment of Intravascular Clotting and Embolism. S. A. Romano.—p. 506.
Rh Factor in Clinical Obstetrics and Gynecology. J. W. Davenport.—p. 510.
Hematuria: Its Clinical Significance. C. O. Frederick.—p. 517.
Management of Prostatism. U. S. Hargrove.—p. 521.

New York State Journal of Medicine, New York

48:961-1088 (May 1) 1948. Partial Index

Radiation Dosage. W. T. Murphy.—p. 1007.
Doctors Beck of Schenectady and Albany. E. Kellert.—p. 1015.
History of Surgery in Rochester, New York. R. A. Leonardo.—p. 1020.
Treatment of Hyperthyroidism with Propyl Thiouracil. S. Rinkoff and M. Spring.—p. 1025.
Optimal Physical Therapy for Rheumatoid Arthritis. E. Stengel.—p. 1028.
Prescription of Occupational Therapy. S. Licht.—p. 1032.
Physical Treatment of "Frozen Shoulder." H. J. Behrend.—p. 1035.

48:1089-1200 (May 15) 1948

Recent Advances in Communicable Disease Control. H. S. Ingraham.—p. 1135.
Chest Injuries. W. Woodruff.—p. 1142.
Diagnostic Sign for Anterior Tibial Vein Thrombosis: Preliminary Report. R. Rosenthal.—p. 1148.
Coronary Artery Disease in Older Patients. G. F. Greco.—p. 1153.
Mycotic Infection in Gangrene of Lower Extremities. S. S. Samuels.—p. 1157.
Penicillin Administration Via The Vagina. R. I. Walter, M. A. Goldberger and Louis S. Lapid.—p. 1159.

Ohio State Medical Journal, Columbus

44:561-664 (June) 1948. Partial Index

Digitalis Intoxication. D. H. Gregor.—p. 593.
Laboratory Diagnosis of Virus Infections. R. F. Parker.—p. 596.
Question of Protein Derangement in Diabetic Retinopathy. G. T. Schwarz.—p. 600.
Reconstruction of Distal Portion of Thumb. E. C. Wechsler.—p. 602.
Nephroptosis. V. C. Laughlin.—p. 604.
Clinical Interpretation of X-Ray Pelvimetry. H. P. Taylor.—p. 608.
Office Gynecology. J. K. Hoerner.—p. 612.
Reduction of Morbidity and Mortality in Lung Abscess by Early Surgical Intervention. A. J. Carlson.—p. 617.
Syndrome of Guillain-Barre: Case Report. J. C. Smith.—p. 621.

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Oklahoma State Medical Assn. Jour., Oklahoma City

41:173-220 (May) 1948

Carcinoma of Body of Uterus. R. A. McGill.—p. 177.
Small Bowel Obstruction. E. E. Talbey.—p. 181.
Surgery of Cervix with Electric Knife. J. E. Wallace.—p. 186.
Chest X-Ray Survey Program in Oklahoma. R. M. Burke.—p. 192.

Review of Gastroenterology, New York

15:439-528 (June) 1948

Infection of Anal Glands. E. T. Whitney.—p. 451.
Postdysenteric Diarrhea Due to Milk Allergy. E. M. Rappaport.—p. 466.
Gastrectomy for Peptic Ulcers. (Based on 350 Gastrectomies.) M. E. Steinberg.—p. 484.
Diseases of Pancreas. (Case Report.) P. D. Badia.—p. 502.
Studies on Dissolved Mucin (Mucoprotein) of Gastric Juice: II. New Quantitative Colorimetric Method for Determination of Total Dissolved Gastric Mucin. G. B. J. Glass and L. J. Boyd.—p. 511.
Oil Soluble Anesthetics in Proctology: Some Old and New Technics. W. Lieberman.—p. 520.

South Dakota Journal of Medicine, Sioux Falls

1:139-178 (April) 1948

Management of Acute Dermatitis. Helen J. Hare.—p. 139.
Renal Tumor. W. A. Dawley.—p. 144.
Distribution of Phosphatase in Human and Mouse Tumors. W. L. Hard, H. R. P. Thomas and M. Belkina.—p. 154.
Use of Intravenous Pentothal in Second Stage of Labor. Mary Price. —p. 159.

United States Naval Med. Bulletin, Washington, D. C.

Supplem. to (March-April) 1948. **Partial Index**

Fundamentals of Isotope Separation. K. Cohen.—p. 6.
Application of Radioisotopes to Problems of Naval Medicine. R. E. Smith.—p. 17.
Thermal Diffusion and Other Physical Methods of Isotope Separation. W. W. Watson.—p. 28.
Pile Production of Radioactive Isotopes. W. E. Cohn.—p. 42.
Production of Radioactive Isotopes by Cyclotron and Other Methods. J. W. Irvine Jr.—p. 52.
New Mass Spectrometer for Isotope Ratio Measurements. H. W. Washburn.—p. 60.
Synopsis of Basic Ideas in Theory of Radioactivity and Detection of Radiation. R. D. Present.—p. 94.
Dosage Levels in Administration of Isotopes to Animals and Man. H. Lisco.—p. 161.

Virginia Medical Monthly, Richmond

75:263-324 (June) 1948

*Results of Vagotomy. S. D. Blackford and A. McCausland.—p. 265.
Diverticulitis of Colon. C. Williams and C. Williams Jr.—p. 269.
*Rhinosporidiosis of Conjunctiva—Case Report. M. Edmunds and Regena Beck.—p. 278.
Treatment of Peptic Ulcer. G. W. Horsley.—p. 281.
Another Fatality Following Use of Tridione and Hydantoin. R. F. Gayle Jr., J. P. Lynch and J. H. Scherer.—p. 288.
Serologic Tests for Syphilis and Their Clinical Application. W. J. Frobhose.—p. 292.
Digitalis in Acute Glomerulonephritis. H. C. Meredith Jr. and J. R. Beckwith.—p. 295.
Sinusitis. F. V. Gammage.—p. 301.

Results of Vagotomy.—Blackford and McCausland report on 22 vagotomies, 12 of which were performed by the transabdominal route in combination with other procedures and 10 of which were done by the transthoracic route without other surgery. In one instance a transthoracic vagotomy was followed two months later by a subtotal gastrectomy with further resection of the vagus nerves. In the 12 patients subjected to transabdominal vagotomy the ulcers were either duodenal or marginal. Vagotomy was combined with subtotal gastrectomy six times, with posterior gastroenterostomy five times, and in 1 case the stomach was opened and the pylorus manually dilated. A three to eleven months follow-up period revealed that results were excellent in 10, good in 1 and poor in 1. There is still insufficient evidence that vagotomy will prevent formation of a subsequent marginal ulcer. Improvement may be the result of the supplementary gastric surgery rather than of vagotomy. Transabdominal vagotomy combined with other gastric surgery must be considered at this stage of clinical experimentation. Transthoracic vagotomy gave equivocal results in the 10 cases reported. In only 6 of the patients have the results been entirely satisfactory. Three patients came to a subsequent subtotal gastrectomy. As yet no criteria have been found by which one can judge which patient having ulcer with pain will be relieved permanently by a simple vagotomy. Until one can predict this and until one knows late results in a large series of cases the authors intend to employ a simple vagotomy with considerable caution.

Rhinosporidiosis of Conjunctiva.—Edmunds and Beck report a case of rhinosporidiosis of the conjunctiva in a white boy aged 12 years. The external appearances of both eyes were normal. When the lower lid of the left eye was everted there was a reddish partially sessile growth originating from the conjunctiva of the lower lid in its outer third. The growth was painless and measured about 6 mm. by 6 mm. by 8 mm. Complete excision and removal of the growth followed by cauterization of the base would seem the best treatment so far available. Microscopic examination of the growth showed a papilloma with little papillary branching or crypts. The striking observation was the presence of numerous round, thick-rimmed, double contoured, sharply defined cystic bodies of various sizes in the stroma of the growth. There was a moderate round cell infiltration around some of the medium-sized cystic bodies and the stroma of the polyp was moderately vascular. These cystic bodies are the trophic stages and immature and mature sporangia of Rhinosporidium seeberi. The spores can be seen being liberated from the sporangium, anywhere in the interstices of the stroma of the polyp, occasionally in the macrophages and in the epithelium. Rhinosporidiosis is a local fungous infection of the mucous membranes with predilection for those of the nose and conjunctiva, caused by Rhinosporidium seeberi. The mode of infection is not known. While this disease appears rather rare, perhaps more cases would be found and diagnosed if more polypoid growths of the nasal mucous membrane, conjunctiva and pharynx were submitted to the laboratory for microscopic study.

Yale Journal of Biology and Medicine, New Haven

20:433-518 (May) 1948

Sir Charles Bell and Mysteries of Brain. E. Podolsky.—p. 433.
Aneurysms of Abdominal Aorta. E. Foord.—p. 441.
*Pregnancy and Thyroid Gland. J. P. Peters, Evelyn B. Man and M. Heinemann.—p. 449.
Immunochemistry of Mouse Tissue Components: III. Comparison of Antigenic Composition of Embryonic Mouse Organs with That of Adult Mouse Organs and With Mouse Tumors. Esther Sylvia Macalla.—p. 465.
Incidence of Primary Atypical Pneumonia of Unknown Etiology. J. R. Gallagher.—p. 473.
Mechanism of Topical Effect of Penicillin G in Experimental Local Streptococcal Infections. E. Grunberg, R. J. Schnitzer and C. Unger.—p. 479.
Concentration Partial Purification, Properties, and Nature of Staphylocoagulase. M. Tager.—p. 487.

Pregnancy and the Thyroid.—Peters and his associates point out that while it is generally agreed that the thyroid gland undergoes hyperplasia during pregnancy, there is no certainty that this hyperplasia is attended by hyperfunction. The rise of basal metabolism in pregnancy is not accompanied by other recognized manifestations of hyperthyroidism. Serum cholesterol is said to increase, a phenomenon that is regularly observed in hypothyroidism. Clinical hyperthyroidism may begin during pregnancy, but this does not seem to be a frequent occurrence. The authors are concerned chiefly with the concentrations of precipitable iodine in the serums of pregnant women. They found that precipitable iodine of the serum rises sharply at the onset of pregnancy from the normal concentration of 4 to 8 micrograms per hundred cubic centimeters to concentrations between 6 and 10 micrograms, and remains at these levels until delivery, after which it rapidly returns to the normal range. This rise is not accompanied by other manifestations of increased activity of the thyroid gland. There is reason to identify the increment of iodine with the thyroid hormone. There is evidence to suggest that failure of the precipitable iodine to rise at the onset of pregnancy leads to early miscarriage which may be prevented by the administration of active thyroid substance. Low precipitable iodine in these cases is not accompanied by other manifestations of thyroid deficiency. The serum-precipitable iodine in pregnancy does not appear to be consistently related to the concentration of iodine preceding pregnancy. No evidence has been found that serum-precipitable iodine is abnormal in women with infertility or toxemias of pregnancy.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

British Journal of Industrial Medicine, London

5:51-106 (April) 1948

Eye Hazards and Safety Practice: Review of 14,722 Eye Accidents in Wearside Shipyards: Preliminary Report. A. Kefalas.—p. 51.
Fibrosis in Lungs of Silver Finisher. H. E. Harding.—p. 70.
Toxicology of Zircon: Preliminary Report. H. E. Harding.—p. 75.
Studies in Occupational Morbidity (2). I. Sutherland and G. P. B. Whitwell.—p. 77.
Boils and Infected Hands: Epidemiological Investigation. G. P. B. Whitwell and I. Southerland.—p. 88.

British Journal of Ophthalmology, London

32:257-320 (May) 1948

Optics of Contact Lenses. A. G. Bennett.—p. 257.
Observations on Pulse and Retinal Arterial Pressure. W. Kapuscinski. —p. 273.
Pterygium. E. Rozen.—p. 300.
Anterior Lenticglobus: An Atypical Case. K. Sen.—p. 305.
Genesis and Operation of Senile Entropion. A. Kettesy.—p. 311.
Note on Physiology of Aqueous Humour. E. Barany and H. Davson. —p. 313.

British Medical Journal, London

1:819-866 (May 1) 1948

Pernicious Anemia of Pregnancy and the Puerperium. L. S. P. Davidson, R. H. Girdwood and J. R. Clark.—p. 819.
*Folic Acid. J. F. Wilkinson.—p. 822.
*Congenital Megacolon: Results of Treatment by Spinal Anesthesia. F. D. Telford and H. A. Haxton.—p. 827.
Megaloblastic Anemia of Pregnancy: Report of Unusual Case. M. Gillespie and A. M. Ramsay.—p. 828.
Hereditary Edema (Milroy's Disease). J. Braham and G. Howells. —p. 830.
Two Cases of Periarteritis Nodosa with Observations on Etiology, Diagnosis and Treatment. J. M. Sutherland.—p. 832.

1:867-916 (May 8) 1948

Histamine. J. H. Gaddum.—p. 867.
"Antistin" in Dermatology. J. Overton.—p. 874.
"Antihistan" in Treatment of Asthma and Hay Fever. N. Southwell. —p. 877.
Chiasma Lesion Due to Fall in Epileptic Fit. R. Klein and P. P. O'Mallie.—p. 880.
Juvenile General Paralysis: Case with Spontaneous but Short-Lived Remission. W. L. Milligan.—p. 881.

Folic Acid.—Wilkinson discusses the effects of folic acid and of the folic acid conjugates, pteroyltriglutamic and pteroylheptaglutamic acids, on hematologic changes. Pteroylglutamic acid produces good hematologic and clinical effects only in macrocytic anemia with some degree of megaloblastic change in the bone marrow; it has little or no effect on patients with normoblastic marrow. Consequently the following types of anemia respond to pteroylglutamic acid: pernicious anemia, macrocytic megaloblastic anemias of pregnancy, infancy, pellagra, sprue, steatorrhea and celiac disease; nutritional macrocytic anemias (with or without nutritional leukopenia), and possibly achrestic anemia. Pteroylglutamic acid acts equally well when given orally or parenterally. The initial dose varies but is usually 15 to 20 mg. a day orally, or 50 to 150 mg. intravenously. In pernicious anemia a prompt reticulocyte response is produced after the administration of pteroylglutamic acid, followed by general hematologic and clinical improvement, but not quite so well or so rapidly as with a highly potent liver extract. A maintenance treatment of 5 to 20 mg. daily is necessary, but after months increased doses may be necessary. Macrocytosis still tends to persist even after one to two years' treatment. Pteroylglutamic acid is of no value in preventing subacute combined degeneration of the cord in pernicious anemia. For this reason it is not a satisfactory treatment for pernicious anemia, and since it has no advantages over present day highly potent liver extracts or stomach preparations, it should not be given alone as routine to patients with pernicious anemia.

Spinal Anesthesia in Treatment of Congenital Megacolon.—Telford and Haxton point out that the idea that megacolon is due to achalasia— i. e., an imbalance between the sympathetic (filling) and the parasympathetic (emptying) mechanism, which results in a relative inadequacy of the latter action—altered the outlook by suggesting an attack on the nerve supply rather than on the bowel itself. In 1935 Stabins, Morton and Scott showed that success followed the use of a spinal anesthetic. A number of successful results have been reported by other workers. These reports are open to criticism in that the follow-up period is too short. The authors reexamined the patients treated by spinal anesthesia between 1938 and 1945. Of the 17 patients treated 11 were reexamined and a detailed report was received of a twelfth one. The results were good in 8 of these patients, fair in 2; the treatment had failed in the other 2. The explanation of the results obtained in the megacolon of childhood from spinal anesthesia remains a mystery, and the method must at present be regarded as purely empiric. For some reason, the shock of the anesthetic abolishes the imbalance between the sympathetic and parasympathetic supply of the colon. One can only assert that the method is simple and that it works. Good results are more certain in young patients. Twelve years seems to be the upper age limit for success. The method is useless in the megacolon of adults, usually mechanical in origin.

Lancet, London

17:1-621-660 (April 24) 1948

Aspects of Old Age. J. H. Sheldon.—p. 621.
Pneumonic Plague in Rangoon. G. Wynne-Griffith.—p. 625.
*Treatment of Tuberculous Meningitis with Streptomycin: A Report to the Medical Research Council. H. V. Smith, R. L. Vollum and H. Cairns.—p. 627.
*Reiter's Syndrome: Report on Nine Cases. R. J. G. Morrison and M. Thompson.—p. 636.
Diabetes Insipidus Due to Sphenoidal Sinusitis: Report of Case. K. P. Ball and A. C. Thackray.—p. 637.

Streptomycin Treatment in Tuberculous Meningitis.—Smith and his associates treated 18 cases of tuberculous meningitis with streptomycin. In 14 the diagnosis was confirmed by culturing Mycobacterium tuberculosis from the cerebrospinal fluid; in 1 confirmation was obtained at necropsy; in 1 acid-fast bacilli were seen and in the 2 remaining patients, both of whom have recovered, the diagnosis was not confirmed. Of the 18 cases, 7 have proved fatal, the illness being prolonged in all but 2. Of the 11 survivors, 7 were treated with streptomycin for sixty-eight to two hundred and fifty-five days and are now virtually free from symptoms, one to six months after their treatment ended. The 4 other survivors are still under treatment, which was begun over two months ago. The dosage for systemic administration in adults was 2 Gm. of streptomycin daily, at first by divided doses and then by a single daily dose. After about four months, if the patient is doing well a single injection of 2 Gm. is given every forty-eight hours. Intrathecal treatment is accomplished by a single daily injection given into the lumbar subarachnoid space or into the anterior horn of the lateral ventricle; for adults 0.1 Gm., for infants 0.05 to 0.075 Gm. Occasionally the streptomycin was also injected into the subarachnoid space in the region of the optic chiasm. Higher levels could be maintained in the cerebrospinal fluid by injecting streptomycin directly into the theca. It is still too early to assess the final results, since the longest survival period to date after cessation of treatment is five months, and relapse or tuberculoma of the brain must be considered a possibility. In the 7 survivors (4 adults and 3 children), who have stopped treatment, the neurologic recovery is complete except for loss of caloric response and high-tone deafness in all 4 adults (children not tested but not obviously deaf). In 1 patient, who had for some weeks severe hemiplegia on the right and aphasia, weakness of the right hand persists, with occasional generalized fits. Ataxia was present in 2 patients during the later stages of treatment but has since almost disappeared. The early functional results in the 7 survivors who have ceased treatment is highly satisfactory, but among these 7 are 3 unverified cases. The authors conclude that the practical value of streptomycin in the treatment of tuberculous meningitis has been established.

Reiter's Syndrome.—Morrison and Thompson say that since the triad of arthritis, conjunctivitis and urethritis was described by Reiter in 1916 little has been heard of this syndrome, but many physicians serving in the Middle East during the late war

were familiar with it as arising in the course of, or during convalescence from, acute bacillary dysentery. More recently cases have been encountered without any apparent connection with dysentery; 9 such cases met with in British troops in Western Germany in a period of nine months are described here. The knee joints were affected in all cases, and the small joints of the hands and feet in some. Two patients had had gonorrhea a few days before the onset of symptoms; in 2 cases there was evidence of prostatic infection, and in 1 urinary infection. Since there was no response to penicillin or sulfathiazole, it was decided to try protein shock, and courses of intravenous injection of T.A.B. (typhoid, paratyphoid A and B) were given to some of these patients. Some benefit seemed derived from this treatment.

1:661-666 (May 1) 1948

Some Reflections on Genius. W. R. Brain.—p. 661.
Function of Cruciate Ligaments of Knee-Joint. A. J. Helfet.—p. 665.
Alendrine and Anthisan in Bronchial Spasm. H. Herzheimer.—p. 667.
*Penicillin Therapy in Scarlet Fever and Complicating Otitis. T. Jersild.—p. 671.
Quantitative Sensitisation of a Penicillin-Resistant Staphylococcus. H. I. Winner.—p. 674.
Anaesthesia in Cardiac Surgery: With Special Reference to Operations for Patent Ductus Arteriosus. B. Rait-Smith and G. Ostlere.—p. 674.
Unusual Cause of Spasm of Psoas Muscle. C. Poniedel.—p. 676.

Penicillin in Scarlet Fever.—Jersild says that at the Blegdam Hospital in Copenhagen a total of 1,000 patients with scarlet fever have been treated with penicillin since December 1945 and have been followed up. It was found that intramuscular injection of 90,000 to 150,000 units of penicillin twice a day will rid the nose and throat of hemolytic streptococci within forty-eight hours. It is unnecessary for this purpose to maintain a bacteriostatic concentration of penicillin in the blood by giving injections every three hours or by injecting the penicillin in peanut oil, wax or epinephrine. To prevent the reappearance of the streptococci the penicillin treatment should be continued for six days. Sore throat subsided rapidly under this treatment. The average febrile period was only four and one-half days compared with seven days in controls treated with sulfanilamide. No complications in the form of otitis or nephritis developed. The average stay in hospital was only eight days. Accordingly, the saving in hospital days was great. The reduction of injections to two daily makes home treatment possible where conditions allow the patient to be isolated for a few days. During the years 1941 to 1945, in spite of energetic treatment with sulfanilamide, up to 38 per cent of patients with scarlatinal otitis had to undergo mastoidectomy. With penicillin therapy, of 56 patients admitted with scarlatinal otitis only 2 required mastoidectomy, and in 1 of these mastoiditis was already present at the start of treatment with penicillin.

1:697-736 (May 8) 1948

Is Rheumatism A Virus Disease? M. Gordon.—p. 697.
*Acute Hematogenous Osteomyelitis: Method of Treatment. F. R. Tucker and C. Hollenberg.—p. 701.
*Primary Atypical Pneumonia: Clinical Study. J. W. Stephens.—p. 703.
Mastoid Surgery—Old and New. A. Tumarkin.—p. 708.
New Antibacterial Diamidines. R. Wein, J. Harrison and W. A. Freeman.—p. 711.

Acute Hematogenous Osteomyelitis.—The procedure which Tucker and Hollenberg have adopted in acute hematogenous osteomyelitis consists of intramuscular injections of 62,500 units of penicillin at three hour intervals for at least twenty-eight days and early surgical treatment, if the patient's general condition will allow it. The results obtained in 10 patients treated with this method are compared with the results obtained in two other groups; the first, consisting of 20 patients, was treated with small doses of penicillin and drainage and the second, comprising 9 cases, was treated only with penicillin. The highest percentage of satisfactory results was obtained in the group of 10 treated by the authors, to whom penicillin was administered in daily doses of 500,000 units for at least twenty-eight days. Early metaphysial decompression in conjunction with a long course of penicillin gives improved results. The erythrocyte sedimentation rate returns to normal within three weeks in the cases which progress favorably; it remains raised in cases which tend to progress unfavorably. There were no deaths in the series.

Primary Atypical Pneumonia.—This report by Stephens is based on 58 cases of atypical pneumonia occurring in troops in the Naples area in March 1946. Since the outbreak was sharply limited in space and time, 75 per cent of cases occurring in the same unit, it is highly probable that the responsible agent was the same in every case. The constancy of the clinical picture was striking. The outbreak was of particular interest because there were factors which suggested an affinity with infective hepatitis: (1) with the onset of the explosive outburst of primary atypical pneumonia, the incidence of infective hepatitis fell to zero, and fresh cases of infective hepatitis occurred in the area only after the subsidence of the epidemic; (2) the uncommon but undoubted enlargement of the liver, and (3) the relatively common complete anorexia, such as only develops in the early stages of infective hepatitis. The possibility cannot be ruled out that some of the febrile cases of anicteric hepatitis were really cases of primary atypical pneumonia. No final conclusion may be drawn from these observations, but they do suggest that the virus causing atypical pneumonia is closely related to that of infective hepatitis.

Medical Journal of Australia, Sydney

1:453-484 (April 10) 1948. Partial Index

Electroencephalography: Localization of Cerebral Lesions. G. Trahair and A. K. Garven.—p. 458.
Primary Atypical Pneumonia. J. S. T. Stevens.—p. 461.
*Observations on Role of Penicillin in Treatment of Haemophilus Influenzae Meningitis. S. Williams.—p. 463.
Occurrence of Rapid Potential Changes in Electrencephalogram. M. H. Draper, R. S. Edgar and W. A. Dibden.—p. 465.
*Diameter of Cardiac Muscle Fibers: Study of Diameter of Muscle Fibers in Left Ventricle in Normal Hearts and in Left Ventricular Enlargement of Simple Hypertension. T. E. Lowe and E. W. Bate.—p. 467.

1:485-520 (April 17) 1948. Partial Index

Some Factors Predisposing to Juvenile Rheumatic Fever in Sydney. Joan Storey.—p. 492.

Penicillin in Haemophilus Influenzae Meningitis.—Williams says that although strikingly good results have been obtained with a combination of the sulfonamide compounds and immune rabbit serum in meningitis due to Haemophilus influenzae, the mortality rate of this disease is still over 40 per cent. At the hospital with which Williams is connected, penicillin has recently been added to these methods of treatment, and it was thought desirable to institute some form of bacteriologic evaluation of its usefulness in this disease. An attempt has been made to relate the penicillin sensitivity of the organism to the concentration of penicillin in the cerebrospinal fluid. Twelve strains of type B H. influenzae showed penicillin sensitivities in the range of 0.5 unit to 2 units per cubic centimeter. Estimations of penicillin in the cerebrospinal fluid of patients with H. meningitis due to influenzae receiving a daily intrathecal injection of 20,000 units of penicillin show that an inhibitory level for these organisms is maintained only for a period of twelve to eighteen hours. It is suggested that intrathecal injections of 20,000 units of penicillin, spaced at intervals of twelve hours, could provide an adequate and continuous bacteriostatic concentration in the cerebrospinal fluid and thus form a useful addition to the existing methods of treatment.

Diameter of Cardiac Muscle Fibers.—Lowe and Bate present a historical survey of the measurements of the diameter of cardiac fibers made since late in the nineteenth century and describe their own studies on 5 microscopically normal hearts from young adults and 2 from adults with simple hypertension without congestive cardiac failure and whose deaths were not due to cardiac causes. The results obtained lead to the conclusion that the uniformity of fiber size in the hypertrophied hearts provides additional evidence for the concept of a "limit hypertrophy" for cardiac muscle fibers, and that there is uniform hypertrophy in each muscle layer of the enlarged hearts. There is uniformity of tension in each muscle layer of the hypertrophied hearts. In the normal hearts, it is perhaps slightly less in the innermost layer of the left ventricular wall, while tension seems to be uniform in the outer layers

Acta Chirurgica Scandinavica, Stockholm

96:393-484 (April 30) 1948. Partial Index

*Surgical Treatment of Essential Hypertension. L. Efskind.—p. 393.
*Two Operatively Treated Cases of Hemangioma of Liver. P. Alsén. —p. 403.
Selective Abdominal Vagotomy. C. Frankson.—p. 409.
Pneumectomy for Pulmonary Metastasis from Cancer of Uterus 10 Years After Hysterectomy. K. Liavaag.—p. 420.
Vitamin K for Balancing of Prothrombin Index in Dicoumarin Treatment. S. Borgström.—p. 431.
Results of Partial and Total Gastrectomy in Cancer of Stomach. E. Landelius.—p. 441.
*Peritoneal Irrigation in Uremia: Report of 3 Cases. B. Fretheim and O. Selvaag.—p. 461.

Surgical Treatment of Essential Hypertension.—Efskind reports 41 cases observed for one to five years after surgical treatment for essential hypertension. The clinical results seem to be stabilized after one year to such a degree that they may be regarded as lasting. The cardiac and cerebral symptoms are so greatly improved that frequently there seems to be a considerable discrepancy between this subjective improvement and the postoperative decrease in blood pressure. In 8 patients the pressure became normal; 16 had a fall in systolic pressure of 60 to 110 mm. of mercury; 7 had a decrease of 30 to 55 mm. and 10 showed little or no decrease. Eighty per cent of the patients showed subjective improvement. Histopathologic alterations were found in the kidneys of 75 per cent of the patients in whom renal biopsies were taken at operation. In 2 patients who died (one as the result of an accident), it was found that although both had had greatly reduced pressure the renal necropsy specimens showed no improvement. Renal arteriolosclerosis and hypertension seem to be independent processes in the earlier stage of their development. The effect of the operative treatment on the blood pressure is most satisfactory in young patients with symptoms of short duration. This fact and the irreversibility of renal changes indicate early operation for this disease. Contraindications are fixed blood pressure and bilateral renal arteriolosclerosis.

Hemangioma of Liver: Surgical Treatment.—According to Alsén hepatic hemangioma of a size to cause discomfort and require operation is rare. Only 67 cases were reported before 1942. The author describes the histories of the 2 patients, women aged 63 and 58 years, respectively, operated on by him. The cavernous hemangioma arose from the right hepatic lobe in one case and from the left in the other. The tumor usually appears in the upper part of the abdomen, usually to the right of the midline, and develops from above downward. It follows the respiratory movements. Its percussion sounds are in direct continuation with those of the liver. Connection with the liver is demonstrable by palpation. The tumor is freely movable from side to side. The tumors arising in the left lobe and which are pedunculate seem to be the easiest to remove. Ligature of isolated bleeding vessels, mass ligature, Paquelin cautery and in some cases packing have been employed to arrest the bleeding. Puncture or incision of the tumor is not advisable because of the great danger of hemorrhage, this being much less if dissection is done in the surrounding healthy liver tissue.

Peritoneal Irrigation in Uremia.—Fretheim and Selvaag used peritoneal irrigation in 3 cases of uremia. Two of the cases were due to anuria following intoxication with corrosive mercuric chloride and sulfathiazole, respectively, and 1 was a result of chronic nephritis. In the case of intoxication with corrosive mercuric chloride the treatment was started after eight and one half days of anuria and continued for three and one half days. A total of 105.5 Gm. of urea was removed and the nonprotein nitrogen dropped from 330 mg. per hundred cubic centimeters to 140 mg. The diuresis started again and complete restitution resulted. The patient who had anuria due to sulfathiazole was moribund and died twelve hours after the treatment was started. Sulfathiazole was removed from the organism simultaneously with the urea. In the case of chronic nephritis with uremia the peritoneal irrigation was continued for seven days. Urea in the irrigation fluid came up to a total of 211 Gm., causing a drop in the nonprotein nitrogen from 480 mg. per hundred cubic centimeters to 133 mg. The electrolytes also tended toward normal values. Clinically, the condition showed astonishing improvement, but rapid deterioration set in after treatment, causing death within three weeks.

Acta Clinica Belgica, Brussels

3:1-116 (Jan.-Feb.) 1948. Partial Index

*Observations on Streptomycin in Treatment of Tuberculous Meningitis. R. Dubois, R. Linz, H. Leschanowski and others.—p. 1.
Malignant Tumors of Testes: Their Radiologic Treatment. J. A. Henry. —p. 75.

Streptomycin in Treatment of Tuberculous Meningitis.—Dubois and his co-workers used streptomycin in the treatment of tuberculous meningitis and in acute miliary tuberculosis beginning November 1946. The authors report on the first 26 patients who were observed during the first five months. Streptomycin was given simultaneously intramuscularly and subthecally. Periods of treatment alternated with periods of rest. The first period of treatment was usually forty-five days. Then followed a rest period of twenty days, then a treatment period of twenty days and another rest period of twenty days; after a third treatment period of thirty days treatment was stopped. Twenty-one of the first 26 patients were still alive at the end of five months, and 19 of them seemed clinically cured and could be discharged into sanatorium care for further convalescence. It appears that the prognosis is the more favorable the earlier treatment is begun.

Helvetica Chirugica Acta, Basel

15:73-160 (May) 1948. Partial Index

*Surgery of Gall Bladder and Emetine. E. Melchior.—p. 75.
Remarks on Twenty Years' Observations on Goiter at Surgical Clinic in Geneva. E. Witzig.—p. 100.
*Is There Tuberculosis or Not? Microscopic Examination or Inoculation? E. Urech.—p. 125.

Surgery of Gallbladder and Emetine.—Melchior used emetine hydrochloride in treatment of 11 patients with severe cholecystitis and 9 patients with calculous cholangitis, complicated by biliary cirrhosis in 2. The dose of the drug varied from 0.03 Gm. given two times per day to 0.05 given two times daily, by subcutaneous or intramuscular route. Treatment was continued for nine to seventeen days with a total dose of 0.5 Gm. to 1.02 Gm. Eight of the 11 patients with cholecystitis received the drug postoperatively, when rise of temperature occurred after cholecystotomy or cholecystectomy. In the remaining 3 cases emetine hydrochloride was given without surgical intervention. Four of the 9 patients with cholangitis were given emetine hydrochloride postoperatively, and to 5 the drug was administered in the absence of any surgical intervention. In the majority of these 20 cases the infection was caused by coli bacteria which are resistant to penicillin. The antibiotic action of emetine hydrochloride appeared to be of importance, as was demonstrated particularly in cases in which the drug was given in the absence of any surgical intervention. The rapid improvement obtained in these grave cases suggests an antitoxic mode of action. Besides the usefulness of this drug in amebic diseases and its suppurative complications, it appears to be valuable in the therapeutic armamentarium in biliary infection. It is not a substitute for surgical treatment since it cannot remove stones or provide sterilization of infected hollow organs, but it makes possible to postpone surgical intervention in cases of grave cholangitis with obstruction until the infection associated with severe icterus and hepatic insufficiency has subsided and temperature has been restored to normal.

Inoculation and Microscopic Examination as Diagnostics of Tuberculosis.—Urech compared the results of inoculations of guinea pigs and those of microscopic examination in 30 cases of abdominal adenitis of apparently tuberculous character. The inoculation yielded positive results in only 6 cases, while cellular lesions of a tuberculous nature were demonstrated on microscopic examination in 28 cases. In a comparative study of these two methods in 5 patients with tuberculous cervical lymph nodes, the inoculation was positive in only 1 instance, while positive results were obtained in 4 cases on microscopic examination. From the clinical point of view the adenitis was extremely active in several of these cases. In a third series of 10 cases various tuberculous materials were collected in the course of surgical interventions on patients in whom tuberculosis was in the active stage. Guinea pigs were infected with this material in 6 instances, while microscopic examination gave positive results in all cases. Further investigations on a large

scale are suggested to answer the question whether the surgeon can rely on positive results of inoculation alone and whether the number of bacilli required for infecting guinea pigs with tuberculosis is as small as it is commonly believed.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

92:969-1048 (April 3) 1948. Partial Index

*Erythema Observed in Undernourished Persons in Internment Camps in Java. D. Brouwer.—p. 976.
*Chronic Lead Poisoning. R. Reisberman.—p. 983.
Tubercle Bacilli in Sputum of Fasting Stomach Contents in Absence of Roentgenologic Changes in Lung. J. C. Gerrits.—p. 988.

Erythema in Undernourished Persons.—Brouwer observed passing eruptions of erythema in underfed internees in camps in Java. The eruptions were sometimes accompanied by high grade fever. These patients had intestinal disturbances, often in the form of bacillary dysentery; also symptoms of vitamin deficiency and hunger edema. A large percentage had disturbances of hepatic function, and the liver was often enlarged. The author discusses the connection between malnutrition and hepatic damage, calling attention to reports of Anglo-Saxon authors on the syndrome of malignant malnutrition in African natives. The author concludes that the erythema described was caused by toxins absorbed from the bowel and not sufficiently detoxicated by a damaged liver.

Chronic Lead Intoxication.—Reisberman observed a man who complained of abdominal pain and was slightly jaundiced. At first, infectious hepatitis was thought of. Then it was learned that this man's wife had been treated for similar disturbance three or four times in the course of the last two years. The mother of this man had similar complaints. The anamnesis revealed that 3 persons living in the same place had died, one of them a child, with coma and convulsions. Chronic lead intoxication had been ascertained as the cause of the disorders in the aforementioned patients. The child had probably died of lead encephalitis. The authors review the results of the urinary lead assays and of the assays of the well water which had supplied the patients, pointing out that the urine of the 2 women patients contained 78 and 115 micrograms per liter, respectively, and the well water contained 125 micrograms per liter, whereas official standards indicate that 39 micrograms is the maximum normal concentration per liter of urine. The author stresses the hepatic damage caused by chronic lead poisoning, which may give the impression of infectious hepatitis.

Nordisk Medicin, Stockholm

38:771-818 (April 16) 1948. Partial Index

Medical Treatment of Peptic Ulcer. F. Hirschberg.—p. 771.
Prognosis in Conservative Treatment of Bleeding Peptic Ulcer. Late Results in 218 Cases. S. Haraldson.—p. 778.
*Spontaneous Hematoma of Abdominal Wall. A. Sanderud.—p. 783.
Foci of Inflammatory Nature in Abdominal Wall. S. Frandsen.—p. 786.
Surgical Treatment of Esophagus Atresia. P. Sandblom.—p. 787.
Determination of Serum Protein by Copper-Sulfate Method. Practical Micromethod. I. C. Højensgard.—p. 797.
Pulmonary Sclerosis. C. F. Jenssen.—p. 802.

Spontaneous Hematomas of Abdominal Wall.—Sanderud says that while spontaneous hematomas of the abdominal wall were described by Hippocrates, Galen and Leonardo da Vinci he has found only 200 cases, mostly in middle-aged and elderly multiparas, published in the literature up to 1946. These tumors, though infrequent, should be borne in mind in uncertain cases of abdominal disease. Their seat is usually below the umbilicus and most often in the rectus muscle, less often in the oblique or the transverse muscle. The cause is rupture of muscle fibers due to indirect relatively insignificant trauma with resulting sudden rapid contraction of the abdominal muscles; in some cases rupture of the inferior epigastric artery and/or vein occurs. Treatment in severe cases is excision, emptying and suture of the musculature, possibly ligature of blood vessels; in milder cases rest in bed for a few days suffices. Uncertain cases indicate operation. Of the 6 cases reported, all in multiparas, 2 were in the oblique muscle, 4 in the rectus muscle. The largest tumor extended from symphysis to umbilicus. In 4 cases the immediate cause was an attack of coughing; in 1, automobiling over rough road, and in 1, unknown. There was acute violent pain in the 5; more gradually developing pain in the sixth. Diagnosis of spontaneous hematoma of the abdominal wall was made in 3 cases and considered in 2; in 1 case operation was done under the diagnosis of ovarian cyst with torsion.

Praxis, Bern

37:357-376 (May 20) 1948. Partial Index

*Streptomycin in Acute Hematogenous Tuberculosis, Miliary Tuberculosis and Tuberculous Meningitis. W. Löffler.—p. 357.
Time Relationship Between Visceral Tuberculosis and Hematogenous Dissemination. H. U. Gloor.—p. 361.
Clinical and Statistical Results of Vaccination with BCG. P. Press.—p. 365.

Streptomycin in Tuberculosis.—Löffler reports on use of streptomycin in acute disseminated forms of tuberculosis, such as tuberculous meningitis and miliary tuberculosis. Satisfactory results were obtained in adults with miliary tuberculosis with 2 to 3 Gm. of the drug administered in four to six fractional doses for twenty-four hours by intramuscular or deep subcutaneous route. In addition, 100 to 150 mg. in 1 to 5 cc. of isotonic solution of sodium chloride or Ringer's solution were given by intraspinal route to patients with tuberculous meningitis. Intracisternal introduction of streptomycin was not practiced except when the lower segment of the lumbar canal was obliterated. Treatment with streptomycin in acute hematogenous tuberculosis was continued for ninety to one hundred and twenty days. After this period streptomycin was administered every second, third or fourth day. Drug resistance develops less readily if large initial doses are employed. Results in 13 cases of meningitis with or without miliary tuberculosis in 8 men and 5 women showed that the effect of the drug depends directly on the early treatment, not later than the twelfth day after the occurrence of meningitic symptoms. In 5 of these patients the bout was controlled; 6 patients showed temporary improvement and 2 were failures. The essential importance of early diagnosis is emphasized. These results were obtained in cases which prior to the streptomycin treatment were considered incurable. Untoward reactions, particularly vestibular disturbances, were noted; as a rule they were only temporary, but deafness may result. Treatment with streptomycin must be followed by prolonged fresh air and rest.

Presse Médicale, Paris

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*Surgical Treatment of Hypertensive Nephropathies. L. and P. Langeron.—p. 349.
Early Diagnosis of Cancer of Esophagus. P. Chase and Merioux.—p. 350.
*Intramuscular Copper Therapy in Chronic Inflammatory Rheumatism. J. Forestier, F. Jacqueline and S. Lenoir.—p. 351.
Injections of Procaine Hydrochloride. R. Herr and R. Riveaux.—p. 352.

Surgical Treatment of Hypertensive Nephropathies.—The Langerons present observations on 23 patients with hypertensive nephropathy. They maintain that in permanent arterial hypertension there always exists a hypertensive nephropathy. The physiopathologic conditions by which the nephropathy maintains and aggravates the arterial hypertension can be improved by surgical intervention. The surgical technics which have been suggested are numerous, but more important than the nature of the intervention is that the one selected be done early. Some forms of hypertension do not require surgical treatment, and even in chronic forms there may be contraindications to surgery such as old age or pathologic conditions in heart and kidney.

Copper Therapy in Chronic Inflammatory Rheumatism.—Forestier and his associates say that whereas at first copper therapy was used in cases of intolerance or resistance to gold therapy, in the last six years indications for its use have been extended in that it has been used in polyarthritis of recent development. At first a copper salt was used, but in 1946 the authors began to use an organic copper compound, cupra-oxyquinoleine sulfonate of methylamine. The authors describe results obtained in 55 patients with chronic inflammatory rheumatism. Thirty of these patients have been observed for two years and 25 others for a year. The administration was by the intramuscular route, 0.5 Gm. being injected two or three times a week. The total dose in a series of injections was between 6 and 9 Gm. No undesirable effects were observed. There is a possibility of alternating this copper therapy with gold therapy or of combining it with orthopedic measures, physical therapy or the use of mineral waters.

Book Notices

Identification of Tumors: Essential Gross and Microscopic Pathologic Features Systematically Arranged for Easier Identification. By N. Chandler Foot, M.D., Professor of Surgical Pathology, Cornell University Medical College, New York. Fabrikoid. Price, $8. Pp. 397, with 241 illustrations. J. B. Lippincott Co., 227-231 S. 6th St., Philadelphia 5, 1948.

The identification of tumors is an important and intricate subject. Every textbook on pathology and many special treatises deal with it. This book offers a new approach. It is fashioned somewhat on the order of the many popular guide books for identification of animals and plants. The material is divided in two main parts, the first of which, 96 pages long, aims to identify tumors of general distribution in eight chapters on tumors of fibrous tissue, cartilage and bone, muscle, fat, serous membranes, cardiovascular system, epithelial and lymphoid tissues. Part two, 255 pages long, deals with tumors of special systems and organs in eleven chapters on respiratory system and mediastinum, alimentary system, liver, gallbladder, pancreas, urinary system, organs of internal secretion, male and female reproductive systems, including breast, nervous system, skin, ear and eye. The source, site, age and sex and gross and microscopic appearance of each tumor are presented briefly and, in some instances, also signs and symptoms, differential diagnosis, metastasis, malignant analogues in the case of benign tumors and prognosis. The heading of the final chapter is "Tabular Locator For Tentative Identification of Neoplasms." Characteristic features are listed in five or six columns with the following headings: characteristic cells (type cell), stroma or matrix, differentiation, mitotic figures, other features (referring to certain special findings, for example, edema, hemorrhage) and chemical admixtures (collagen, mucin, calcium). The last column offers the diagnosis. This sort of diagnostic key is an interesting experiment. Its efficacy is difficult to judge until it is tested on persons uninitiated in diagnosis of neoplastic diseases. It is at least a good beginning in the right direction of systematizing microscopic diagnosis of tumors. There is also a 10 page chapter with the author's choice of fixation and staining methods.

The presentation is clear, though necessarily brief. Wise economy of words has made it possible to put in a wealth of information in a relatively small amount of space. The illustrations are instructive and well chosen and executed, with only occasional defects.

The book is a major contribution by a distinguished authority. Dr. Foot's long experience as successful teacher and his outstanding contributions to pathology are reflected in the monograph. Pathologists, especially those in the early phase of their development, will profit by having this book within reach when attempting to interpret microscopic slides of neoplastic lesions. It may also be used advantageously by the medical student and young physician for general orientation and clarification in a difficult subject.

Modern Drugs in General Practice. By Ethel Browning, M.D., Ch.B. Second edition. Cloth. Price, $4. Pp. 223. Williams & Wilkins Co., Mount Royal and Guilford Aves, Baltimore 2, 1947.

This book is at best suitable only for physicians practicing in England because of the frequent reference to trade names familiar in that country. While the author claims that no proprietary preparation is mentioned unless the claims have been substantiated in medical literature, it is unusual for an author to acknowledge advertising material by saying "I should, however, like to express my thanks to those manufacturers of certain preparations mentioned who have put at my disposal literature containing their own claims which are supported by clinical reports."

Although this book is a second edition, it is out of date for the practitioner. For example, the section on penicillin is inadequate and there are no discussions on the newer antibiotics. Also found wanting is the chapter on the sulfonamide compounds. And discussions of the newer agents such as the antihistaminics are lacking entirely. Other criticisms could be raised—for example, concerning the use of gold in the treatment of tuberculosis—but the book does not merit such lengthy review.

Children's Hospital [Denver]: A History of Achievement and Progress from 1910 to 1947. By John W. Amesse, M.D. Cloth. Pp. 95, with illustrations. The Children's Hospital Association, Denver, Colorado, 1947.

In 1897 a small outdoor clinic housed in tents operated during the summer months in Denver for deserving children without fee. The clinic was closed the following year on account of the Spanish-American War, but in 1906 the project was revived by a group of resourceful women who raised the funds. In 1908 articles of incorporation were signed by four members of the group under the name of the Children's Hospital Association. Thus was originated the great Children's Hospital of Denver. The author reviews the history of this institution as written by Mrs. George Packard, up to 1934, and brings the history on through the year 1944. He points out the steady growth from a small beginning into a 250 bed hospital with clinics, laboratories, libraries, blood bank, isolation unit, training school for nurses, physical therapy, occupational therapy and social service and the Boettcher School which offers educational opportunities to long term patients.

The opening chapter is a brief account of children's hospitals in other cities and countries. The first hospital in this country devoted exclusively to children was the unit at Philadelphia founded in 1855 with only 12 beds and which has since become not only a great hospital but a leading research institution. The second hospital limited to pediatrics was that of Boston founded in 1863; then followed children's hospitals in New York, Albany and San Francisco, Detroit (1877), St. Louis (1879), Chicago (1882) and Louisville (1891). Today there are some forty-four hospitals for children in the United States with 4,770 beds, and these figures do not include the separate departments or wards for children attached to practically all general hospitals throughout the United States.

The Rehabilitation of the Patient: Social Casework in Medicine. By Caroline H. Elledge, Assistant Professor of Social Work, McGill University, Montreal. With a foreword by Philip D. Wilson, M.D. Cloth. Price, $2.50. Pp. 112. J. B. Lippincott Co., 227-231 S. 6th St., Philadelphia 5, 1948.

As medical science has become more complex, it has become more difficult for the physician to treat the patient as well as the disease. The busy medical specialist has neither the time nor the training to give full consideration to all the personal, psychologic, social, economic and vocational aspects. To meet this need, there has been an increasing use of the medical social worker as a member of the therapeutic team. The author, who is an assistant professor of social work at McGill University, presents the importance of the nonmedical problems of the rehabilitation of the severely handicapped and shows how the medical social worker can aid in their solution. Through the case presentation method, the author deals with such problems as the emotional attitude toward disability, employment and family relationships, illustrating the varying methods of approach and technics used by the medical social worker. As pointed out by Dr. Philip D. Wilson in his foreword, some readers may object to the almost 100 per cent success of the medical social worker in solving the problems presented in the case histories. All, however, after reading the book, should agree on the need for the medical social worker on the rehabilitation team. An interesting book for the physician and others concerned with services to the handicapped, this is primarily a book "of the medical social worker, by the medical social worker and for the medical social worker."

Handbook of Treatment and Medical Formulary. By Charles M. Gruber, Ph.D., M.D., Professor of Pharmacology, Jefferson Medical College, Philadelphia. Fabrikoid. Price, $7. Pp. 585. F. A. Davis Co., 1914-16 Cherry St., Philadelphia 3, 1948.

This book essentially is devoted to the treatment of various medical problems arranged alphabetically. The descriptions are brief, although statements on symptoms and physical findings are included for many of the diseases. The drugs proposed for treatment are usually presented as prescriptions. Official compendia and New and Nonofficial Remedies obviously have been used and respected by the author, although occasionally there may be examples of remedies that might be questioned by some clinicians. The book is too brief for use other than quick reference. It is not intended, however, as a voluminous source of information; references are included for those desir-

ing additional details. Obviously there are some who insist that comparatively brief outlines are inadequate for use by the student and practitioner, but, such books often provide information which is needed quickly. Furthermore, there are many persons who wish to be informed concerning what is usually an effective treatment, leaving details concerning other measures that occasionally are worthy of trial to more leisurely moments for reading. If such limitations are kept in mind, books intended as somewhat terse guides are often helpful.

Clinical Laboratory Methods and Diagnosis: A Textbook on Laboratory Procedures with Their Interpretation. Volume I; Volume II. By R. B. H. Gradwohl, M.D., D.Sc., F.R.S.T.M.& H., Director of the Gradwohl Laboratories and Gradwohl School of Laboratory Technique, St. Louis. Volume III: Parasitology and Tropical Medicine. By R. B. H. Gradwohl and Dr. Pedro Kouri, Director, Institute of Tropical Medicine, Havana. Fourth edition. Cloth. Price, $40. Pp. 1295, with 403 illustrations; 1297-2411, with 330 illustrations; 804, with 427 illustrations. C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, 1948.

This comprehensive textbook on laboratory procedures has now been increased to three volumes. The general purpose of the book has been to assemble and describe accepted laboratory procedures and the interpretation of these procedures in the light of diagnostic medicine. The book is a guide and a reference work that will be most useful to workers in laboratory and clinical medicine. New authors have been engaged especially for the rewriting of certain sections of the book, such as Dr. Oscar Felstenfeld for the chapter on bacteriology, Dr. Julius Elson for a new chapter on the technic of electrocardiography, Dr. J. J. Weinstein for a chapter on protein metabolism and parenteral protein hydrolysate and Dr. Afrania do Amaral of Brazil for an authoritative section on scorpionism and aranetism. The section on the Rh factor supplies up to date knowledge relating to these important laboratory technics. A section has been included on the diagnosis of cancer by vaginal smears from the work of Papanicolaou and others.

A special effort has been made to supply for this edition accurate indexing and cross indexing for quick reference work. Many excellent plates and diagrammatic representations are included. The chapters on toxicology and on police crime methods are particularly interesting and have been completely revised. The added third volume on parasitology and tropical medicine appears especially good and useful in view of the increasing numbers of these tropical diseases found in the United States.

Clinical Diagnosis by Laboratory Methods: A Working Manual of Clinical Pathology. By James Campbell Todd, Ph.B., M.D., Arthur Hawley Sanford, A.M., M.D., Professor of Clinical Pathology, Mayo Foundation, University of Minnesota, Rochester. With the collaboration of George Giles Stilwell, A.B., M.D., Division of Clinical Laboratories, The Mayo Clinic, Rochester, Minnesota. Eleventh edition. Fabrikoid. Price, $7.50. Pp. 954, with 397 illustrations. W. B. Saunders Co., 218 W. Washington Sq., Philadelphia 5, 1948.

With the eleventh edition, this well known book has been available to the medical profession for nearly forty years. Dr. Sanford, the present author, became associated with the original author, Dr. Todd, during the preparation of the sixth edition and since then has maintained its high standards. With the present edition, Dr. Sanford has completely revised the book with the help of various associates at the Mayo Clinic. Several new chapters have been added and the book has been completely rearranged. The former chapter on serodiagnostic methods has been divided into three short chapters. The material on mycology has been made into a separate chapter. New cuts and plates have been added. A number of old illustrations have been dropped from the text, but the number remaining is larger than in any previous edition. While the number of pages continues to increase, the book is still of convenient size.

Coronary Heart Disease. By A. Carlton Ernstene, M.D., Chief of the Section on Cardiovascular Disease, Cleveland Clinic, Cleveland, Ohio. Publication No. 16, American Lecture Series. Fabrikoid. Price, $3.50. Pp. 95. Charles C Thomas, 301-327 E. Lawrence Ave., Springfield, Ill., 1948.

This monograph presents in lecture form the author's views on coronary heart disease including angina pectoris, acute myocardial infarction, acute coronary failure, paroxysmal cardiac dyspnea, heart block with disturbances of cardiac rhythm, congestive heart failure and the risk of anesthesia and surgical operations with patients with coronary disease. The material is presented in a fairly elementary form, obviously being designed for physicians who wish a review of the subject, medical students, interns and resident physicians. The sections on diagnosis are satisfactorily complete and should be helpful, especially since the author uses the actual phrases that patients frequently use to describe their symptoms. Sections on etiology and pathology are brief and to the point. The discussion of the electrocardiographic changes is fairly satisfactory, but for a subject which requires mental visualization as the reader attempts to picture the electrocardiographic changes described, the omission of suitable electrocardiographic examples is a loss to the reader. The therapeutic procedures used today in the treatment of heart diseases, including coronary heart disease, are matters of difference of opinion even among leading cardiologists. It is not surprising, therefore, that the author finds himself on the horns of a dilemma regarding some of his therapeutic recommendations. For example, he states that no one has ever shown a real improvement of angina by the use of either alcohol or aminophylline, but after this concludes that one should use aminophylline but not alcohol. The rationalization for the recommendation of a sodium-free diet and mercurial diuretics in the treatment of angina is questionable, as are statements that papaverine has a sedative action and that patients with fresh coronary disease should be atropinized. Other controversial points include the use of plasma in the treatment of shock associated with coronary thrombosis and the contraindication of the use of cyclopropane in cases of shock or heart failure. The discussions of the use of quinidine are good, and the author describes with detail and accuracy the use of anticoagulants, particularly "dicumarol," in the treatment of coronary thrombosis. This book will have its main value to beginners in the field of cardiovascular diseases.

Por nuestro niños. Cuido y protejo a su niño. . . la tuberculosis ataca a la niñez! Por el Dr. Luis F. Romaguera, director del Dispensario. Paper. Pp. 47, with illustrations. Municipio de la Habana, Departamento de sanidad municipal. Dispensario de vias respiratorias, Habana, [n. d.].

This booklet, published in Spanish by the Health Department of the City of Havana, is a series of short articles illustrated by cartoons dealing with the prevention of disease. The first cartoon shows the three major elements in combating tuberculosis; namely, air, light and water. The following article has to do with poor milk and other factors in the spread of tuberculosis, including a rather horrible cartoon showing how the disease may be spread. This cartoon has been ingeniously designed to show how everything possible could be wrong in a street scene, including exposed food, milk distribution from cans, the shaking of dusty rugs above uncovered food and the hanging of meat in the open, unprotected against flies. To complete the scene there is a coughing victim of pulmonary tuberculosis, another on crutches representing white swellings, and another in a pushcart representing Pott's disease. The suggestions for hygienic living are in small cartoons around the edges. Other topics touched on include the iniquities of the house fly, the importance of good teeth, the role of alcohol in tuberculosis, the evils of spitting and sneezing, the virtue of open air play and many other hygienic and epidemiologic factors.

History of Factory and Mine Hygiene. By Ludwig Teleky, M.D. Cloth. Price, $4.50. Pp. 342. Columbia University Press, 2960 Broadway, New York 27, 1948.

Out of the smoke of pre-war Germany has come a book which speaks to stir the imagination of those who believe that health economies in design and production can be effected in America by increased governmental control. Dr. Teleky, an apparent advocate of "romance in type," informs his readers that factory health inspection in the United States is inferior to the German system. He mentions that American industrial health personnel are not well trained, and bemoans that there is heavy resistance to compulsory health insurance. The volume contains 13 chapters, including a summary, a bibliography and an index, heavy with foreign references. Readers of this book should clearly understand that Ludwig Teleky was for some years identified with the German way of doing things.

Synopsis of Pediatrics. By John Zahorsky, A.B., M.D., F.A.C.P., Professor of Pediatrics and Director of the Department of Pediatrics, St. Louis University School of Medicine, St. Louis. Assisted by T. S. Zahorsky, B.S., M.D., Senior Instructor in Pediatrics, St. Louis University School of Medicine. Fifth edition. Fabrikold. Price, $5.50. Pp. 449, with 167 illustrations. C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, 1948.

In the fifth edition of this well known volume of pediatrics, some minor alterations have been made in keeping with recent advances. Some of the newer drugs are only mentioned; i. e., diphenhydramine ("benadryl"). There are 158 text illustrations, of which many are from the original edition. Some of these are obsolete, as for example the illustration of the technic for intramuscular injection of blood into the buttocks in hemorrhagic disease and icterus gravis. This present edition will continue to be a most practical and useful manual for the busy general practitioner.

Psychotherapy: Its Uses and Limitations. By D. Rhodes Allison, M.D., M.R.C.P., and R. G. Gordon, M.D., D.Sc., F.R.C.P. Oxford Medical Publications. Cloth. Price, $3. Pp. 160, with 1 illustration. Oxford University Press, 114 Fifth Ave., New York 11; Amen House, Warwick Sq., London, E.C.4, 1948.

The aim of this book is well stated in the preface. The authors have, they say, "tried to point out how without special knowledge the physician and the family doctor may often help the patient to conquer his disease by maintaining his courage and morale, and have urged the necessity, if medicine is to progress, that an end should be made to suspicions and rivalries and that all branches of medicine should combine to fight disease in a team which can deal with both psyche and soma with individual and environment, all of which indeed are indivisible." Some of the chapter headings are: psychosomatic conditions, the relation of rheumatism to mental illness, psychotherapy in the treatment of psychoses, the patient's reaction to bodily disease, and the combined approach.

The authors recognize the value of psychotherapy in certain well selected cases, pointing out that it is no panacea, that no one method is applicable to all cases, and that the personality as well as the training of the therapist is important. They point out, too, the fallacy of blaming on the patient's "uncooperativeness" any failure of therapy; instead, they say, "it is the business of the doctor to determine, if he possibly can, why the patient cannot or will not cooperate, and in the case of the psychoneurotic, to resolve the difficulty or to hand the patient over to some one who can do so [p. 148]." The authors write well, with eminent British common sense and broadness of view. The book can be recommended to every physician interested in the field of treatment.

Chaucer's World. Compiled by Edith Rickert. Edited by Clair C. Olson and Martin M. Crow. Cloth. Price, $6.75. Pp. 456, with illustrations selected by Margaret Rickert. Columbia University Press, 2960 Broadway, New York 27, 1948.

This scholarly volume began with the research of the late Professor John M. Manly and Edith Rickert on Chaucer and Chaucer's times. The book includes a collection of documents, quotations, diaries, notebooks and all sorts of other memorandums which afford a fascinating reflection on the times concerned. A section dealing with the ethics of the physician has already been quoted in the Tonics and Sedatives column of THE JOURNAL. There are several other medical items of similar interest. Most of the quotations in medicine come from the famous John Arderne, who was born in 1307 and whose work seems to have been personally known to Chaucer. There is record of a case of malpractice for wrongly setting an arm with a claim for damages of 200 pounds. The record of the Court of Common Pleas of the London of that period seems to have involved the doctors rather frequently.

Barbed-Wire Surgeon. By Alfred A. Weinstein, M.D. Cloth. Price, $3. Pp. 310. The Macmillan Company, 60 Fifth Ave., New York 11, 1948.

In 1940 Dr. Alfred A. Weinstein joined the United States Army. Thereafter he was nearly three and one-half years in prison, sometimes in hospitals, under the none too gentle care of the Japanese. Reports indicate that some 18,000 were under these tender ministrations but about 4,000 survived to return home. The record by Dr. Weinstein is an account of the situations in which he took an actual part. It is full of incidents and anecdotes with a medical flavor and it will serve to remind both those who fought and those who remained at home that the brutalities of the Far East were quite as vicious as those of middle Europe and had their own peculiar flavor as well. As the author says in his prologue, this is the story of GI Joe in prison, a story of hunger and disease, in which the personal problems of the author serve to carry the thread of the story from beginning to end.

Life is for Living. By D. Ewen Cameron, M.D., Professor of Psychiatry, McGill University, Quebec. Cloth. Price, $2.75. Pp. 241. The Macmillan Company, 60 Fifth Ave., New York 11, 1948.

The trend toward writing interpretive books for lay people continues. However, the quality of many of these works is so poor that the lay reader becomes more confused than settled in his thinking. Dr. Cameron apparently is the newest aspirant to attempt to climb the bandwagon of popular psychiatric works. His title is intriguing, but his material is disappointing. He states that he has written a book for those of us who are trying to grope our way through the confusions and contradictory absurdities, the moral dangers and the psychologic pestilences of midcentury living. The organization of the book is in itself confusing, because there seems to be no planned continuity in the development of his concepts. At certain points the text is even incoherent. He raises many questions and then goes off into rambling, philosophical answers which could not satisfy even the most learned seeker for stability. The author uses the text to present some of his favorite concepts without documentation. The book does not have either index or bibliography. The author closes with a trite statement that "what we must do is to see our world. . . . in which we must at last take final responsibility for ourselves, in which all man's works will be his works."

Symposium on Medicolegal Problems Under the Co-Sponsorship of the Institute of Medicine of Chicago and the Chicago Bar Association. Edited by Samuel A. Levinson, M.D., Ph.D., for the Committees of the Institute of Medicine and the Chicago Bar Association. Fabrikold. Price, $5. Pp. 255. J. B. Lippincott Co., 227-231 S. 6th St., Philadelphia 5, 1948.

The Institute of Medicine of Chicago and the Chicago Bar Association collaborated in 1945 in arranging a symposium on medicolegal problems. Six subjects were selected for discussion, and the medical and legal aspects of each subject were presented respectively by a physician and by an attorney, followed by a question and answer period. The subjects chosen were The Medical Witness in Court, Artificial Insemination, The Practice of Pathology and Its Medicolegal Problems, Operations to Produce Sterility, Trauma and Tumors in Industrial Medicine, and Scientific Tests in Evidence, such as blood grouping tests in disputed paternity cases and chemical tests for intoxication. This small volume contains the twelve papers that were presented and the discussion that followed the presentations. These papers are most informative, and the symposium concretely reflects the value of meetings between groups of physicians and lawyers for discussions of ofttimes perplexing problems of mutual interest. Physicians, lawyers and others interested in this particular field will find in these papers much of value and answers to many questions that cannot be found conveniently elsewhere.

An Introduction to Clinical Psychology. Edited by L. A. Pennington, Ph.D., Associate Professor of Psychology, University of Illinois, Urbana, Illinois, and Irwin A. Berg, Ph.D., Associate Professor of Psychology, Pomona College, Claremont, California. With a foreword by George D. Stoddard, Ph.D., President of the University of Illinois, Urbana. Cloth. Price, $5. Pp. 395, with 43 illustrations. The Ronald Press Co., 14 E. 20th St., New York 10, 1948.

The authors point out that the variations in what clinical psychologists individually do accounts for marked differences in content of courses labeled "clinical psychology." There are many state certification laws which require academic credit for a course in clinical psychology. Yet students who meet this requirement frequently secure widely differing training in different institutions. Such courses may actually be those of advanced abnormal psychology, psychologic and clinical testing or a minor course in counselling and psychotherapeutic technics. Still a fourth course may be concerned solely with personality development. The aim of this book is in a sense to alleviate these difficulties and present a first course in clinical psychology, including a definition, meanings of concepts, a discussion of

behavior problems, presentation of the tools with which the psychologist works, a description of minor therapeutic procedures by which behavior disorders can be alleviated and a discussion of professional relationships between psychologists and members of the psychiatric profession and their mutually overlapping fields.

Certain sections of the discussion revolve about the problem of where the field of the psychologist ends and that of the psychiatrist begins. The authors appear to hold to the view of nonlimitation of the field of the psychologist, which is directly in contradistinction to the attitude of most psychiatrists and psychoanalysts. Most psychiatrists feel that the function of the clinical psychologist in therapy of mental disease is to render assistance to the psychiatrist, rather than to assume his whole function. The volume is otherwise excellently conceived and provides a comprehensive coverage of clinical psychology, especially for the student. Fifty-six useful illustrations and reference tables are included.

A Textbook of Clinical Pathology. Edited by Francis P. Parker, M.D., Associate Professor of Pathology, University of Virginia School of Medicine, Charlottesville, Virginia. [Formerly edited by Ray R. Kracke and Francis P. Parker.] Third edition. Paperbound. Price, $9. Pp. 1025, with 329 illustrations. Williams & Wilkins Co., Mount Royal and Guilford Aves., Baltimore 2, 1948.

This new edition represents a revision of the previous one by Kracke and Parker. The contents are made up of contributions by eight authors, all authorities in their branches of clinical pathology. As in previous editions, the interpretation of laboratory findings is the most distinctive feature and is of special value to practitioners.

The chapter on blood includes technic and findings of bone marrow studies. In the discussion of hemorrhagic diseases the procedures helpful in diagnosis and treatment are well described. Blood groupings and Rh factors are particularly well discussed and brought up to date. The section on clinical chemistry emphasizes the common determinations, including phosphatases, total proteins, sodium and potassium. Short chapters on an assay of hormones and vitamines have been included. Tests for hepatic function, including the valuable cephalin-flocculation and alkaline phosphatase tests, are assembled separately. Sputum examinations are well illustrated and include examinations for fungi and the fluorescent demonstration of acid-fast organisms.

In a brief chapter, the tests for renal function are presented in clear, simple form. Illustrations of slide and tube agglutinations, cutaneous reactions in allergy and brucellosis add to the clear, comprehensive presentation of immunologic tests in disease.

With reference to the serologic diagnosis of syphilis, the additional procedures like the Mazzini slide test and Boerner-Lukens complement fixation test are described. Biologic false-positive reactions and their interpretation are discussed.

In the appendix is a valuable description of the common bacteriologic technical methods employed in a hospital laboratory. Each chapter is supplemented, in most instances, by an adequate bibliography.

The book is recommended to students and practitioners as well as laboratory personnel for its interpretive as well as informative contents.

Neuroanatomy. By Fred A. Mettler, A.M., M.D., Ph.D., Associate Profesor of Anatomy, College of Physicians and Surgeons, Columbia University, New York. Second edition. Cloth. Price, $10. Pp. 536, with 357 illustrations. C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, 1948.

This is the second edition of a work which first appeared in 1942, a fact which is ample evidence that the book has met with approval. The book is divided into two sections. The first half deals with the gross anatomy of the nervous system, exclusive of the peripheral nerves. The sympathetic system is briefly discussed. The second half is concerned with the microscopic organization of the nervous system and a limited correlation of structure with function. The facts of neuroanatomy are, for the most part, presented accurately. They are not always readily available and their relationships and significance are often not made apparent to the beginning student, for whom the book is written. The index contributes to the difficulties in locating the desired information. Many titles have a large number of pages cited without any qualifying references; the vagus nerve has 59, the medial lemniscus 54 and other titles almost as many. With these the reader can waste much time before locating the principal discussions. Furthermore, the discussions of many subjects have been divided between a number of different places. Much of the discussion of the detailed structure of the central nervous system, notably the brain stem, is by description of successive serial sections. These are detailed and accurate. However, the attempted correlation of this information is so incomplete that the student must have difficulty in appreciating the organization of any extensive system. In not a few places the discussions are unduly complicated and at the same time deficient. The description of the gross anatomy of the trigeminal nerve on page 81, of the interventricular foramina of Monro on page 104 and of the efferent and afferent connections of the cerebellum on pages 326 to 327 are cases in point. The extensive, careless use of inaccurate contractions of terminology, characteristic of the dissecting room and laboratory, detracts from the book. Examples of this are the repeated use of "dura" for "dura mater," of "callosum" for "corpus callosum" and of "medulla" or "oblongata" for "medulla oblongata." There are a few obvious errors, such as the following: the trigeminal (or gasserian) ganglion does not lie in the floor of the cavernous sinus (page 81). The posterior commissure does not end in the pineal body (page 100). The rubrospinal tract in man is not comparable to that in lower animals as the student would probably conclude from page 345. The origin of specific extrapyramidal corticofugal pathways is not discrete and sharply localized as is indicated in figure 263A. This work is profusely illustrated. There are a number of clear, illustrative photomicrographs, and 46 pages of well chosen references to the literature.

American Universities and Colleges. Edited by A. J. Brumbaugh, Vice President, American Council on Education, Washington, D. C., and Mary Irwin. Fifth edition. Cloth. Price, $8. Pp. 1054. American Council on Education, 744 Jackson Place, Washington 6, D. C., 1948.

Among the most valuable of the reference books available in the field of education is this standard guide first inaugurated in 1928 and thereafter published at four year intervals. The book is up to date and includes complete facts regarding 820 educational institutions with all of the information that the average student or any one else in the educational field would wish to have. The appendixes provide full information concerning the American Council on Education and other educational associations, information concerning academic costumes and accepted abbreviations for degrees. There is also an extensive general index, institutional index and a series of classifications by geographic and other divisions.

Directory of Physicians Interested in Clinical Allergy. Compiled by Jonathan Forman, B.A., M.D., F.A.C.A. Fabrikoid. Pp. 176. The Compiler, International Correspondence Society of Allergists, 856 Bryden Road, Columbus 5, Ohio, 1948.

This book contains a list of physicians who devote all or a part of their time to the treatment of allergic patients. The names are listed by states, cities and countries. The compilers admit that there may be omissions and welcome additions, corrections and suggestions for the next edition. Brief data concerning membership in professional societies accompany many of the names. The two indexes in the back comprise an alphabetical list of allergists in the United States and an alphabetical list of allergists in other countries. The several full page advertisements might well have been placed at the front or back of the book.

Taking the Cure: The Patient's Approach to Tuberculosis. By Robert G. Lovell, M.D. Cloth. Price, $2. Pp. 93, with 6 illustrations by Donald Gooch. The Macmillan Company, 60 Fifth Ave., New York 11, 1948.

This booklet is packed full of sound advice for the tuberculous patient from one who has been through the mill. It has a special appeal in its brevity, its coverage of pertinent information and advice and its all-around excellence of quality. It is easily readable and may serve both the well read and those of more limited cultural attainments. The message is punctuated by a few well placed and impressive caricatures. There is also a useful bibliography for tuberculous patients which in reality will serve every type of human mentality.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

VITAMIN C IN ACUTE RHINITIS

To the Editor:—Massive doses (1,000 mg. the first day; 700 mg. the second) of ascorbic acid have been recommended in the early stages of acute coryza, and the claim has been made that an acute cold may be aborted by this form of therapy. Is there evidence either for or against this form of therapy? Do harmful effects occur from therapy with ascorbic acid in the mentioned dosage?

M.D., New York.

ANSWER.—A few years ago several articles appeared which advocated use of large doses of ascorbic acid in the early stages of acute rhinitis. Subsequently little evidence has appeared to support the contention that this therapy has any appreciable effect in aborting or cutting short the attack. Personal experience also fails to support the claim. Harmful effects have not been reported or experienced by the writer. More recently the use of tripelennamine hydrochloride or other antihistaminic drugs has been recommended in the early stages of acute rhinitis on the assumption that vasodilatation responsible for the free flow of nasal secretion could be controlled by these drugs. Beneficial effects are reported by a few persons, but controlled statistics are not as yet available.

CATALEPTIC RIGIDITY

To the Editor:—A school of hypnology (so-called) issues a prospectus wherein there is a picture of a 235 pound (106.6 Kg.) man standing on a 113 pound (51.3 Kg.) woman in a cataleptic state supported by her heels and her head. Must I believe this? Would she support a ton? For how long? We know that a certain degree of tonic rigidity can be secured in a cataleptic state but surely the cataleptic patient cannot become as rigid and strong as a plank of hard wood.

Max Isenberg, M.D., New York.

ANSWER.—Under deep hypnosis a subject can be given the suggestion that he will become rigid and the subject's body will retain the position in which it has been placed for a considerable time, even when the attitude is one which is difficult to maintain. It is quite possible that a woman of 113 pounds could support, in a cataleptic state, a man of 235 pounds for a few seconds. Under continued tension the muscles of course may eventually give way. This would depend on the musculature of the individual. Although a subject may remain rigid indefinitely this rigidity would not be maintained under a great weight. Such a person would not be able to support a ton, and no person would likely be able to maintain twice his or her weight more than a few seconds. The potential strength of the subject's muscles and bones would be the determining factor, and not the hypnotized will.

LEAD POISONING AND ARTERIOSCLEROSIS

To the Editor:—A patient, 58 years of age, has had chronic lead poisoning of eight to ten years' duration. There is a history of a lead line, typical colics, weakness, peripheral pain without paralysis, typical blood picture and normal blood pressure without evidence of renal involvement. The urine has always been entirely normal and there has been no peripheral edema. A few years ago symptoms of a peripheral occlusive vascular disease of the right leg developed which was diagnosed elsewhere as Buerger's disease and also as endarteritis obliterans. A progressive change occurred which led to gangrene requiring amputation. Now it is claimed that the occlusive vascular disease which required the amputation was due to the chronic lead poisoning. It is my understanding that this does not occur in lead poisoning without associated renal damage. Allen, Barker and Hines in their book "Peripheral Vascular Diseases," page 337, stated, "certainly lead poisoning cannot be considered to be a factor in the great majority of cases of arteriosclerosis and there is considerable question as to whether it ever produces typical arteriosclerotic lesions." Does chronic lead poisoning with normal renal function and normal blood pressure ever produce a peripheral occlusive vascular disease sufficient to cause gangrene requiring amputation?

William W. Locke, M.D., Chicago.

ANSWER.—It is highly unlikely that lead causes arteriosclerosis or accentuates an existing one. Persons exposed to a lead hazard do not appear to have more arteriosclerosis than similar groups of workmen in other trades. As in this patient, the blood pressure appears unaffected by lead poisoning. Arteriosclerotic gangrene is not a manifestation of lead intoxication.

SIZE OF BRAIN

To the Editor:—Please send me details of method of calculating size of living brain based on three linear dimensions of head, as described in Berry's "Brain and Mind," Macmillan, 1928.

M.D., Pennsylvania.

ANSWER.—Berry's method is to obtain measurements of (1) length of head; this is a caliper measurement from the most prominent point of the glabella to the most distant point in the midline at the back of the head; (2) breadth of head, the greatest distance obtainable by the calipers applied to the parietal eminences; (3) height of head, the highest point of the cranium vertically above the center of the external auditory meatus; these measurements are in millimeters and are applied to the following formula:

$$\text{Brain capacity} = 0.000337 \times (\text{length} - 11 \text{ mm.}) \times (\text{breadth} - 11 \text{ mm.}) \times (\text{height} - 11 \text{ mm.}) + 406.01$$

The subtraction of 11 mm. from each of the three measurements is the allowance made for the thickness of the skull and the over-all soft parts. The multiplication of the first four numbers with the addition of the fifth is believed to give the capacity of the brain in cubic centimeters.

TULAREMIA ENCEPHALITIS

To the Editor:—A patient had early papilledema, some sensory changes and a tendency to weakness of the left side of the body. Brain tumor was diagnosed and the patient was referred to a neurosurgeon. Diagnosis was confirmed and operation performed. Nothing was found except encephalitis which was believed to be due to an old case of tularemia. What treatment can be given this man? Would any of the biologicals such as streptomycin offer hope? Would roentgen therapy be of benefit?

Dan Raney, M.D., Linton, Ind.

ANSWER.—Infection of the brain in tularemia has been reported, but in this region of the country it must be rare. The difficulty would lie primarily in substantiating such a diagnosis. Localized encephalitis from other sources has been confused with tumor for the reason stated in the question. However, encephalography, or, what would be probably better in this case, ventriculography, would have ruled out a space-occupying lesion. As far as is now know, neither streptomycin nor high voltage roentgen therapy would be of any avail against the bacillus of tularemia. The best treatment would probably be attention to general health and hygiene with, perhaps, iodides in fairly large doses.

HEREDITY OF BIRTH MARKS

To the Editor:—Recently a young primiparous woman gave birth to a female infant with a "port wine stain" occupying the entire lateral surface of right foot, leg, vulva and neural area. The baby was otherwise normal. The mother is considerably upset over this birth mark and has asked for sterilization, even though the couple desires more children. Neither parent nor known relatives have birth marks. What are the chances of a second baby's having similar marks?

Louis H. Spear, M.D., Ottawa, Kan.

ANSWER.—Birth marks or nevi are of many different types. Some of them have been shown to have some hereditary basis, occurring at times in three or four generations. Cockayne, "Inherited Abnormalities of the Skin and its Appendages," (New York, Oxford University Press, 1933) is a good source for detailed information on the subject. Many cases of birthmarks, of the type described, however, appear singly in families; i. e., without evidence of a hereditary basis. Therefore it appears reasonable that the probability of a second child's showing a similar condition is low. Sterilization is hardly indicated.

SPERMATOZOAN IMMUNITY

To the Editor:—A patient requests information on the possibility of temporary sterility of the wife by injection of the husband's semen. I have never heard of the idea and know nothing of it. Neither have several gynecologists whom I have consulted.

M.D., California.

ANSWER.—A good deal of experimental work has been done on animals with the aim of producing a so-called sperm immunity in the female. Injection of spermatozoa, both from the same and from other species, has evoked antibodies which can immobilize and agglutinate spermatozoa in vitro. But in most of the experiments reported the female animals thus "immunized" have continued to breed with undiminished fertility.

A few similar attempts have been made in human beings, with generally inconclusive results. Since neither the degree nor the duration of the possible immunity to pregnancy can be predicted, this method would appear to be among the most unreliable of contraceptive technics.

PNEUMOTHORAX IN PNEUMONIA

To the Editor:—Could pneumothorax be the cause of death in a patient 45 years of age who died twenty-six days after the onset of lobar pneumonia?

W. B. Shore, M.D., Anchorage, Alaska.

ANSWER.—Pneumothorax could be the cause of death of any one regardless of age, or of immediately preceding pneumonia, as a result either of the so-called pleural shock or of extreme displacement of the mediastinum; and in pneumonia or other disease, by reducing further the available amount of aerating lung tissue. Atelectasis during lobar pneumonia is not uncommon, but pneumothorax is rare and occurs chiefly as a result of perforation by secondary pulmonary abscess or empyema. An instance of spontaneous pneumothorax during pneumonia is illustrated in "The Pneumonias," by H. Reimann, Philadelphia, W. B. Saunders Company, 1938, page 91.

Artificial pneumothorax was once used as a therapeutic measure for lobar pneumonia and for a brief time in the 1930's was popularized by Blake. The subject is discussed in "Pneumonia," by R. Heffron, New York, the Commonwealth Fund, 1939, on pages 611, 749 and 769.

"PERMUTIT"

To the Editor:—Please give information or references to use of "permutit," said to be a chemical which removes salt from a normally ingested diet, making a salt-free or salt-poor diet unnecessary in cardiorenal and hepatic cases.

Willis P. Baker, M.D., Santa Ana, Calif.

ANSWER.—During the war a number of compounds were tried for their effectiveness in the desalination of sea water. Among the various substances studied were certain resins or ion exchange materials and zeolites, or "permutit." For example, a sodium or calcium resin in gastric juice would adsorb the hydrogen ion and give off sodium, whereas an acid resin in the intestine would adsorb sodium, magnesium, potassium and calcium and give off hydrogen ions. Zeolites or certain inorganic materials act analogously.

W. Dock (*Tr. A. Am. Physicians* 59:282, 1946) used a resin made by the American Cyanamid Company which in 2 ounce (56.7 Gm.) amounts would remove the sodium in 3 Gm. of sodium chloride. One generally thinks of "permutit" as being an inorganic material, but at a recent meeting of the American Chemical Society it was reported that "permutit Z" was used to adsorb sodium (Abstracts, 113th Meeting Am. Chem. Soc., Chicago, April 19-23, 1948, p. 2c). "Permutit Z" is actually an ion exchange resin made by the Permutit Company which adsorbs not only sodium, but also magnesium, potassium and calcium.

The use of the ion exchange resins orally for the absorption of sodium is now under laboratory investigation. Acid resins should not be used therapeutically now unless the physician is prepared to study the mineral balance of his patient.

SCLEROKERATOSIS

To the Editor:—A young matron, aged 34, has had, since the age of 8, four recurrences of tuberculer scleritis and keratitis. Each attack has been prolonged in course and has been treated by rest and gradually increasing doses of old tuberculin. She has never had evidence of other tubercular lesion despite thorough examination and roentgenogram of the chest at each attack and occasional observation in the intervals. This patient has just had a recurrence for which the described treatment has been given. Has there been any recent development in the treatment of tubercular eye conditions which would improve on this regimen? Is streptomycin of any use in this condition?

W. F. MacDonald, M.D., Schenectady, N. Y.

ANSWER.—The local treatment for sclerokeratosis is atropine sulfate 1 per cent to 3 per cent, twice daily to keep the pupil fully dilated. Cases resistant to the usual treatment sometimes respond to beta rays or Grenz rays. The dosage of beta rays is a total of 175 to 200 per cent erythema dose given over four to six weeks in one course, which may be repeated. The dosage of Grenz rays is 452 roentgens filtered through 0.024 mm. of aluminum twice a week for five treatments. The systemic treatment for sclerosing keratitis is salicylic acid 20 grains (1.29 Gm.) every three hours for five doses. If the diagnosis of tuberculosis is made by subcutaneous injection of old tuberculin a course of therapeutic tuberculin may be given. Streptomycin has not been reported as used clinically. However, streptomycin could be used in 0.5 Gm. doses twice a day, and one should try to give a total dose of 65 Gm. if one believes that the patient would not experience damage to the vestibular branch of the eighth nerve.

ALOPECIA IN WOMEN

To the Editor:—A 38 year old married white woman began losing her hair about eighteen months ago. Thinning has been generalized, but most pronounced in the vertex and frontal regions. Loss of pubic or axillary hair has not occurred. About one year ago she noticed moderate growth of hair on the upper lip, legs and forearms. Menopause occurred at age 36. Her general health has always been good. History is essentially negative. Two brothers were prematurely bald in their late twenties. Examination reveals the following: The scalp is clean, almost shiny. The hair is coarse and dry. Numerous broken hairs can be seen. The skin is of normal texture for one of her age. A noticeable but not prominent growth of hair occurs on the upper lip. The patient is about 15 pounds (6.8 Kg.) overweight. She is alert and appears to be emotionally well balanced. The blood pressure is 130 systolic and 88 diastolic; pulse rate 80; temperature 98.6 F. The Kahn reaction was negative. The red blood cell count was 3,900,000; the hemoglobin 88 per cent. Basal metabolic rate has not been obtained. At the present she is receiving thyroid, 1 grain (0.06 Gm.) daily. Suggestions for therapy and further investigation are requested. Is there rationale for use of pituitary extract in a case of this kind?

M.D., Texas.

To the Editor:—In excessive loss of scalp hair in a 42 year old woman, without other consequential symptoms, associated with an endocrine factor? Some loss of hair—beyond physiologic amount—has occurred for the past ten years, but lately this has become greatly accelerated. No dermatologic condition of the scalp exists. The hairs are thin and break off easily in ordinary combing. The frontal and occipital regions in particular have become devoid of much hair. No definite area of alopecia exists, but there is a general thinning of hair over the entire scalp. Associated excessive loss of hair or growth does not occur at present anywhere else on the body. There has been some hypertrichosis of the face in the past. 1. Can nervous or mental strain be an etiologic factor? 2. Would a past history of high cervical radiculitis with roentgen therapy (over eight years ago) account for excessive loss of hair now? 3. This condition is not familial in the patient's family. What is the prognosis for recession or progression? 4. How commonly do women under 50 have to use transformations because of excessive loss of hair not due to disease of the scalp? 5. Is stimulating scalp treatment of value?

M.D., California.

ANSWER.—Apparently both of these patients have male pattern baldness, which is relatively rare in women. Students of the subject generally agree that in the production of common baldness many factors play a role, particularly androgenic influences and heredity. According to Osborn's study, common baldness is inherited as a sex-limited trait dominant in men and recessive in women, and it is directly inherited from father or mother to son even though the mother herself is not bald. When the inheritance is duplex, baldness appears in women. Hamilton has pointed out that the lack of baldness among eunuchoid men, the subsequent development of baldness in these men after treatment with androgenic substances, and the presence of male pattern baldness in women with adrenal virilism or arrhenoblastoma are all evidence indicative of androgenic influence.

All women with male pattern baldness, therefore, should be examined for evidence of endocrine abnormalities, particularly of the adrenal glands. In the first patient, it would be well to determine the basal metabolic rate before administering more thyroid substance. Sufficient reason does not appear in this case to administer pituitary extract. In the second patient, it is unlikely that nervous strain is playing a role in the production of her baldness, nor would a history of cervical radiculitis treated with roentgen rays eight years previously be a factor. In general, the prognosis is decidedly guarded, for such baldness may rarely progress to the point where a transformation has to be worn. Treatment with stimulating measures is usually worth the effort expended: massage either with the fingers or an electric device; "hair tonics," i. e., scalp lotions containing a rubefacient, and suberythema doses of ultraviolet rays. For these 2 patients, it might also be well to institute therapy with estrogenic substance.

ALASKA ASTHMA

To the Editor:—What is the incidence of asthma in Alaska? Are people who go there from the Ohio area for example benefited or made worse?

P. C. Reed, M.D., Columbus, Ohio.

ANSWER.—Statistics on the incidence of asthma in Alaska are not available. The likelihood of benefit to an asthmatic person from Alaska climate is dependent primarily on the type of asthma. If the asthma is due to such seasonal allergens as ragweed pollen or mold the chances for relief are excellent. If city smoke and dust are known to be potent factors in the individual case, improvement in Alaska is likely. On the other hand, if the asthma is perennial or of the infectious type, or aggravated by damp or cold weather, the Alaskan climate may aggravate the condition. In many instances the factors involved are so indeterminate that only an actual trial residence can settle the issue.

PEPTIC ULCER

To the Editor:—Do ulcers of the stomach, or peptic ulcers, occur in absence of gastric hydrochloric acid? A patient was told by a consultant that he had an ulcer and anacidity, and dilute hydrochloric acid was prescribed.

A. B. Hooton, M.D., Otar, S. C.

ANSWER.—Assuming that a small ulcerative lesion of the stomach is actually present, as verified by the clinical history and roentgenologic examination, the absence of free hydrochloric acid, especially after stimulation with histamine, would make necessary the exclusion of carcinoma in particular, also gastric syphilis, tuberculosis or lymphogranulomatous lesion. With a stimulus like the Ewald meal or its modifications, the lack of free hydrochloric acid in the gastric contents is occasionally noted, even in the presence of an active benign ulcer, especially on single aspiration. Under the circumstances it would be inconsistent to prescribe hydrochloric acid, assuming the presence of a roentgenologically demonstrable gastric lesion.

SECRETORY OTITIS MEDIA

To the Editor:—A patient had recurrent attacks of serous otitis media for two years, and a fluid level would be seen behind the ear drum. This was treated, as the recurrence appeared, by paracentesis with a 20 or 22 gage needle and suction. After aspiration, the ear would remain free for three to four weeks, then the fluid would gradually accumulate. Finally roentgen examination of the mastoid showed mastoid involvement, and a simple mastoidectomy was performed. The cells were broken and filled with debris. The operation apparently was done completely and the area healed nicely except that there was a moderate amount of drainage of this serous material. It was kept open for a while and finally allowed to close. There was a prompt reappearance of the serous material behind the ear drum. Consultation has not helped, and we are thinking of making a permanent perforation of the ear drum in the hope that while this will not prevent the formation of the fluid it will at least allow it to drain whenever it forms. I would appreciate some help on this problem.

Leonard Yaffe, M.D., Baltimore.

ANSWER.—Serous otitis media, or as is more often called, secretory otitis media, is generally due to obstruction of the eustachian tube with resulting negative pressure in the middle ear cavity and accumulation of serous transudate. Removal of the obstruction to the eustachian tube may result in spontaneous resolution. If the fluid has been present for some time, a paracentesis of the tympanic membrane may be necessary to assure resolution. Where the condition exists without visible pathologic change at the mouth of the tube, it is frequently on an allergic basis. Eosinophils can be demonstrated in the serous fluid in such cases. Until the underlying allergy is discovered and removed, the condition tends to recur. The history, cutaneous tests and particularly the use of elimination diets should be employed to find the offending substances.

RECURRENT ERYSIPELAS

To the Editor:—What is the prevention of recurrent erysipelas of the right arm in a woman who has had nine attacks in five years following a right radical mastectomy? Moderate lymphedema occurs. Dermatophytosis is absent. Streptococcus vaccines, both stock and autogenous, have not been of value, nor has 70 per cent alcohol applied to the skin.

Milton Kissin, M.D., New York.

ANSWER.—The fact that erysipelas is noted for its tendency to recur would indicate that treatment aimed at inducing immunity is somewhat less than satisfactory. Several authors, however, report good results from the use of Streptococcus erysipelatis toxin and they stress the importance, too, of eradicating foci of streptococcus infections in sinuses, teeth and tonsils. Treatment with toxoid may be worth a trial in this case. In the past, foreign proteins, such a typhoid vaccine and milk, have had their advocates. If the patient should suffer another attack of erysipelas, it would be well to treat her with huge doses of antibiotics and for a longer period than is usual.

CATARACT

To the Editor:—I have opacities in both lenses with visual loss of about 50 per cent. What is the present status of operation of the soft lens?

M.D., California.

ANSWER.—Whenever the vision is decreased by the lent opacity sufficiently to interfere with the patient's daily life a surgical operation for removal of the opacity is justifiable. The amount of useful vision in a cataractous eye varies with the patient's work, mental attitude and temperament. If a decided handicap results with only a slight decrease in vision the operation is advisable.

It is unnecessary to wait until the cataract becomes more mature as was the previous custom.

EFFECTS OF SMOKING

To the Editor:—I have recently been told that my symptoms suggested an occlusive arterial disease in my feet and that a possibility of coronary insufficiency exists. My doctor advised that I stop smoking. I am aware that this is the usual advice, but I needed some scientific evidence to convince myself of the necessity of the giving up a lifelong pleasurable habit, and so tried to look up the subject. In five standard texts on the practice of medicine, the only reference to tobacco, smoking or nicotine was a short sentence stating that a toxic amblyopia results from tobacco. What is the effect of smoking cigarets? If the practice is harmful, how does one treat withdrawal symptoms? Is the resulting nervousness less harmful than the practice of smoking, especially in coronary disease?

M.D., California.

ANSWER.—The effect of smoking cigarets on the circulation of the lower extremities has been shown to be deleterious in a person who already has a deficient circulation. Cigarets are especially bad, since they are generally inhaled. It has been shown that smoking reduces the amount of blood going to the feet by a considerable amount. Only one way to stop smoking is effective, and that is to stop it 100 per cent. The withdrawal symptoms are not harmful and should not effect coronary heart disease. Lampson reported some investigations on the effect of smoking on the lower extremities and showed a diminution in blood flow for several hours after smoking cigarets. This was published in THE JOURNAL (**104**:1963, 1935). Maddock and Coller also reported peripheral vasoconstriction after smoking (*Ann. Surg.* **98**:70, 1933). Little question exists that tobacco smoking, especially cigarets, does produce a certain degree of vasoconstriction. There is such a large margin of safety in the normal person that this degree of vasoconstriction does not cause any serious effects. However, in a patient with a diminished arterial circulation any decrease in the amount of blood flow reaching the extremity, caused by even a slight degree of vasoconstriction, may be sufficient to produce serious effect. There is little if any evidence at hand that tobacco causes constriction of the coronary blood vessels. However, Theis and Freeland (*Ann. Surg.* **113**:411, 1941) reported that smoking in patients with thromboangiitis obliterans caused a greater reduction in the oxygenation of the blood than in the normal person. This observation if true might indicate that it is also deleterious in patients with coronary disease. It would appear that the majority of evidence is that tobacco smoking is harmful for patients with peripheral vascular disease. The benefits derived from cessation of smoking far outweigh deleterious effects that might be produced by the withdrawal of smoking.

CRYPTORCHISM

To the Editor:—In the May 15, 1948 issue of The Journal is a query concerning a case of bilateral cryptorchism in a man of 21, with complete azoospermia. The inquirer's question is whether hormone therapy is advisable or surgery is indicated.

In connection with your answer, "Unless the patient has some evidence of endocrine dysfunction, there is no indication for any hormonal therapy and a bilateral orchiopexy is indicated," I want to call your attention to the generally accepted routine procedure in cases of cryptorchism, which is to try to cause the testicles to descend by endocrine therapy before resorting to surgery, i. e., orchiopexy, which is acceptable only in mechanical obstacle to descent. Since in this case, the testicles are retained in the abdominal cavity, the surgical intervention (in addition to the operative risk) may prove harmful to the glands, particularly if and when a short pedicle will have to be elongated, with a possibility of complete and permanent atrophy of the glands.

P. M. F. Bishop (*Guy's Hosp. Rep.* 94:12-74, 1945), considers it well to administer a preoperative course of endocrine therapy, not only to insure development of the testis, but also to assist in lengthening the cord, if necessary. I think it is indicated in the inquirer's case because of such evidences of hypogonadism as complete azoospermia and considerable overweight (Froehlich's type of hypogonadism).

S. I. Mavitt, M.D., Los Angeles.

DEXEDRINE

To the Editor:—The claim of Dr. G. Raymond Johnson of Ottumwa, Iowa, in Queries and Minor Notes, The Journal, June 19, page 736, that "dexedrine" produced diabetes in one patient is invalid, in view of your comment that no evidence exists which supports this opinion. We question your statement that diabetic symptoms may be aggravated by the drug and that diabetes is a contraindication to its use.

In a study just completed, we found no instance of aggravation of diabetes by "dexedrine" in a series of 55 obese diabetic patients. In fact, 31 of these patients presented improvement as measured by the glucose tolerance test or by reduction of insulin requirement. The improvement noted in carbohydrate tolerance was probably the result of dietary restrictions and weight reduction. Clinically, "dexedrine" appears to have no direct effect on the diabetes or its course.

Henry Dolger, M.D.,
Kermit E. Osserman, M.D., New York.